Potential Effectiveness and Cost-Effectiveness of Smoking Cessation Counselling and Nicotine Replacement Therapy Coverage in Reducing Smoking-Attributable Lung Cancer Burden in Urban China

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Background: China is in the early stages of the smoking epidemic, and has yet to experience the peak of smoking-attributable disease burden. If current trends continue, annual deaths from tobacco use will increase from the current estimate of 0.67 million to 2 million deaths by the year 2025. However, the rate of smoking cessation in China is low. Currently, there are no population-level smoking cessation interventions widely promoted in China. Given that the tobacco industry is a state-owned monopoly in China that has contributed between 7 to 11 percent of government revenue over the past 15 years, economic concerns are one of the major barriers to a greater promotion of smoking cessation interventions in China.

Objectives: The objective of this study was to use evidence on the effectiveness of physician counselling and nicotine replacement therapy (NRT) patches use from Western countries, with the most recent smoking data from China to predict the potential effectiveness and cost-effectiveness of physician counselling and NRT patch in the healthcare system in urban China.

Methods: In Study 1, statistical analysis was conducted to estimate smoking and cessation rates in urban China. In Study 2, a Comparative Relative Assessment model was used to estimate the effectiveness and cost-effectiveness of physician counselling and NRT patch use for smoking cessation. Study 2 determined the estimates and costs of additional quitters and avoided lung cancer deaths from the implementation of physician counselling and NRT patch use in the healthcare system in urban China. The following four smoking cessation scenarios were examined in Study 2:

- Scenario 1: Brief counselling to ALL smokers;
- Scenario 2: Motivational interview to ALL smokers NOT intending to quit;
- Scenario 3: Intensive counselling to ALL smokers intending to quit;
- Scenario 4: Intensive counselling to only the smokers intending to quit AND being either medium/heavy smokers (CPD>10).

Results: In Study 1, smokers intending to quit were significantly more likely to have quit at follow-up than those not intending to quit. A total of 35.4% of smokers in urban China reported visiting a doctor in the past 12 months. Smokers who visited a doctor were significantly more likely to intend to quit and to have quit smoking at follow- up compared to those who did not visit a doctor. Among smokers visiting a doctor, there were no gender differences in intention to quit. In Study 2, brief counselling to all smokers (Scenario 1) visiting the healthcare system in China was the most effective and cost-effective smoking intervention by generating a total of 2.35 million quitters at $2.32-$7.73 per quitter. All three counselling scenarios were found to be cost saving when compared with the total cost of lung cancer to Chinese society. Due to current high retail prices of NRT patches in China, the wide promotion of the NRT patch would be costly, requiring significant financial investments.

Conclusions: In order to avoid the upcoming smoking-attributable disease and economic burden, the Chinese government will need to promote smoking cessation interventions to smokers. Given the relatively low cost, implementing smoking cessation counselling in the healthcare system in urban China will result in cost savings from lung cancer. The high retail price and low acceptance of NRT patches in China suggest that more time and resources may be required to achieve a population-level impact from pharmaceutical interventions.

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Chapter 1 Literature Review

1.1 Background

1.1.1 Worldwide Overview

Worldwide, the only two large and growing causes of death are smoking and HIV infection. Cigarette smoke contains more than 4,000 chemicals, of which over 60 are known carcinogens (World Health Organization [WHO], 2011). According to the WHO, smoking is a risk factor for six of the eight leading causes of death in the world, including lung cancer, chronic obstructive pulmonary disease (COPD), ischaemic heart disease, cerebrovascular disease, lower respiratory infections, and tuberculosis (WHO, 2008). It is estimated that approximately 5.4 million premature deaths per year globally are attributable to smoking, and more than 80% of these deaths occur in developing countries (WHO, 2008). If the current smoking trend continues, the smoking-attributable death will increase to 8 million per year by 2030.

Smoking is still an increasing global public health issue; however, the smoking epidemic varies substantially across countries and regions. As indicated in Figure 1 (Lopez, Collishaw, & Piha, 1994), a "smoking epidemic" in a specific population usually develops in four stages: an increase and then decline in smoking prevalence, followed three to four decades after by a similar trend in smoking-attributable diseases.

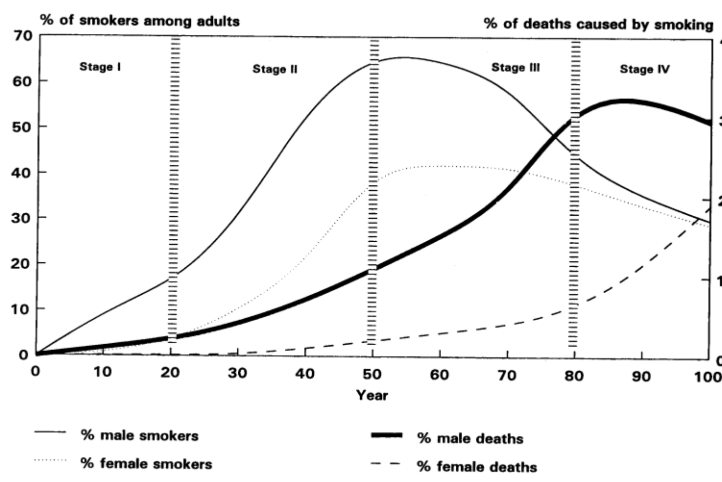


Figure 1.1: Stages of Worldwide Tobacco Epidemic

For many developed countries, such as the US and Canada where cigarettes have been used widely for several decades, both the smoking prevalence and smoking-attributable mortality have passed the peak and are in decline. However, in contrast to the reduction in smoking prevalence among developed countries, tobacco use is growing rapidly in the developing world. According to recent data from WHO (2008), nearly two-thirds of worldwide smokers live in ten countries, including China which alone is home to approximately 350 million smokers who consume nearly one third of the world's annual tobacco (Yang, Fan, Tan, Qi, Zhang, & Samet, 1999).

Developed countries differ greatly from developing countries not only in smoking prevalence, but also in cigarette consumption patterns and smoking cessation rates. Patterns of smoking, smoking cessation, and smoking-attributable disease burden are highly context-specific. For example, in the US and Canada, the overall smoking prevalence is 20.8% (US Department of Health and Human Services [USDHHS], 2010) and 16.7% (Reid, Hammond, Burkhalter, & Ahmed, 2012), respectively. With the widely implemented smoking cessation interventions, approximately half of ever smokers in the US and 60% of ever smokers in Canada have quit smoking (Centers for Disease Control and Prevention [CDC], 2009; Reid et al., 2012). In contrast, in China, the most populous developing country, the smoking prevalence is about 31.4% (Yang, Ma, & Liu, 2005), and the proportion of ever smokers who have quit smoking is only 10% (Qian, Cai, Gao, Tang, Xu, & Critchley, 2010). Research shows that more than 70% of current smokers in China do not report an intention to quit (Yang et al., 2005, Yang, Ma, Chen, Zhang, Samet, & Taylor, 2001).

Cigarette consumption among current smokers is also a key factor associated with smoking cessation rates and smoking-attributable disease burden. Available evidence indicates that cigarette consumption among smokers is a strong predictor of their smoking abstinence (Vangeli, Stapleton, Smit, Borland, & West, 2011). Nicotine uptake increases with the number of cigarettes smoked per day in a dose-dependent way (Blackford, Yang, & Hernandez-Avila, 2006; Law, Morris, Watt, & Wald, 1997; Lubin, Caporaso, Hatsukami, Joseph,& Hecht, 2007). Due to the addictive nature of nicotine, daily cigarette consumption is a reliable indicator of smokers' nicotine addiction level (Lubin et al., 2007). The smokers who consume more cigarettes per day are typically more addicted to smoking, which thereby increases the difficulty of quitting smoking. Few studies have examined the nicotine dependence level of smokers in China; however, the available evidence suggests that in China more than half of current smokers (51.6%) smoke more than 20 cigarettes per day (Qian et al., 2010). The high proportion of smokers that smoke more than 20 cigarettes per day partly explains the low smoking cessation rate in China.

Currently, the two primary tobacco control approaches are smoking prevention among non-smokers and smoking cessation among current smokers. Many available tobacco control measures, such as public education, cigarettes taxes, advertising and marketing restrictions, and smoking bans, reduce smoking by discouraging young people from starting to smoke (Farrelly, Pechacek, Thomas, & Nelson, 2008). Although smoking prevention among non-smokers is the most effective tobacco control strategy in the long term, for current smokers, smoking cessation is a priority because it not only prevents non-smokers from second hand exposure, but also reduces the risk of smoking-attributable disease. Existing evidence suggests that people who quit smoking, regardless of their age, are less likely to die from smoking compared with those who continue to smoke (CDC, 2005; Huxley, Jamrozik, Lam, Barzi, & Ansary-Moghaddam, 2007). The benefits of quitting are most evident for younger smokers aged 25 to 34 years old, but are still significant among older smokers aged 45 to 54 years old who quit later in life (Doll, Peto, & Boreham, 2004). Smokers who quit smoking before the onset of major smoking-attributable disease avoid most of the excess negative health effects of smoking (Doll et al., 2004).

1.1.2 Smoking and Smoking Cessation in China

China has the highest cigarette consumption of any country worldwide, and is home to 350 million smokers (Yang et al., 1999). Despite the huge smoking population, China is at the early stage of the smoking epidemic, and smoking will continue to rise if no effective smoking control intervention is applied. Generally speaking, smoking in China has followed a similar pattern as Western countries, but about 40 years behind.

There are several national studies estimating smoking prevalence in China, but the findings vary by the survey year and by the types of measures used to assess smoking. Appendix A shows the available evidence on smoking prevalence in China from national studies. Overall, smoking prevalence appears to have declined slightly in the last decade. The “ever smoking” rate in China was estimated as 37.6% in 1996 (Yang et al., 1999), then declined to 35.8% in 2002 (Yang et al., 2005), and further declined to 27.7% in 2003 (Qian et al., 2010). Trends in the current smoking rate in China show a decline from 35.3% in 1996 (Yang et al., 1999) to 31.4% in 2002 (Yang et al, 2005) to 26.0% in 2003 (Qian et al., 2010), and a modest increase to 28.1% in 2010 (Li, Hsia, & Yang, 2011). As Appendix A indicates, the measures of smoking prevalence used across studies are inconsistent, thereby suggesting that the decline of smoking prevalence might be partly due to the bias from different measures. However, Qian et al. (2010) investigated trends in smoking prevalence in China by using the 1993, 1998, and 2003 waves of the National Health Service Survey. The findings indicated a clear decline in ever smoking prevalence and current smoking prevalence. In contrast to the decline in smoking prevalence, the proportion of "heavy smokers" in China increased. In 1998, the prevalence of heavy smokers who smoked more than 20 cigarettes daily was 26% and 16% among male smokers and female smokers, respectively (Qian et al., 2010). The prevalence of heavy smokers approximately doubled in 2003 to 53% and 29% among male smokers and female smokers, respectively. The average daily cigarette consumption was stable at about 15 cigarettes daily in recent decades (Li et al., 2011; Qian et al., 2010; Yang et al., 1999; Yang et al., 2005).

Smoking cessation is not common in China. Recent studies indicate over 60% of Chinese smokers do not intend to quit over the next 2 years (Qian, Rao, & Gao, 2009), or would not consider quitting at all even after viewing a warning label on cigarette packs (Yang, Li, Wang, Hsia, Yang, & Xiao, 2010). According to the 1996 National Smoking Prevalence Survey (Yang et al., 2001), a total of 2% of ever smokers in China successfully quit smoking, where success is defined as quitting smoking for at least 2 years. The proportion of quitters among ever smokers increased to 5.7% in China in 2003 (Qian et al., 2009). The quit rate among Chinese smokers is positively associated with older age (55 years or older), having chronic disease, and overall poor health (Qian et al., 2009). Among former smokers, the most frequently reported reasons for quitting smoking were getting sick (36%) and disease prevention (28%).

The use of smoking cessation aids is rare in China. About 98% of Chinese smokers who had attempted to quit did so on their own without using any formal assistance (Luo, 2009). Approximately 20-40% of smokers reported receiving doctor's advice on smoking cessation (Jiang, Ong, & Tong, 2007) and only 5% of former smokers quit because of doctor advice (Qian et al., 2009). The use of smoking cessation medication is even less common. Recent research evidence (Yang, Hammond, Driezen, O'Connor, Li, & Yong, 2011) found only 5.8% of smokers used nicotine replacement therapy (NRT) or/and Zyban.

1.1.3 Lung Cancer and Smoking

Lung cancer has been the most common cancer in the world for several decades. Worldwide, lung cancer incidence and mortality are three times higher in men than in women (Parkin, Bray, Ferlay, & Pisani, 2005). By 2008, it was estimated that 1.38 million deaths were due to lung cancer alone (18.2% of the total) globally, in which 55% were in developing countries (Ferlay, Shin, Bray, Forman, Mathers, & Parkin, 2010). Cigarette smoking is estimated to cause 85 to 90% of lung cancers in the US (Thun, Henley, Burns, Jemal, Shanks, & Calle, 2006).

Lung cancer has been the most common cancer globally since 1985, both in terms of incidence and mortality (Siegel, Ward, & Brawley, 2011). Worldwide, lung cancer contributes to 12.4% of new cancer diagnoses and 17.6% of total cancer deaths. The increase in the number of cases of lung cancer in developing countries is more apparent (Siegel et al., 2011). Among males, lung cancer was the most commonly diagnosed cancer and the leading cause of cancer death in 2008 globally, while for women, lung cancer was the fourth most commonly diagnosed cancer and the second leading cause of cancer death (Jemal, Bray, & Center, 2011). Overall, lung cancer accounted for approximately 1.38 million or 18.2% of total cancer deaths worldwide in 2008 (Jemal et al., 2011).

The WHO (2008) estimates that worldwide lung cancer deaths will keep increasing, largely as one of consequences of increasing tobacco use, especially in Asia. Tobacco use is the primary risk factor for lung cancer (WHO, 2008). A large proportion of all pulmonary carcinomas are attributable to the effects of cigarette smoking (Parkin, Pisani, & Lopez, 1994). Lung cancer is mainly diagnosed among people above middle age. Research indicated that the incidence of lung cancer rapidly increases with age, with no cases diagnosed among people younger than 20 years old, approximately 1.7% of cases under 44 years old, 30% of cases between 45-64 years old, and about 68% of lung cancer cases in people older than 65 years old (Howlader, Noone, & Krapcho, 2010). Lung cancer is among the most lethal cancers. Despite the availability of new diagnostic and genetic technologies, advancements in surgical techniques, and the development of new biological treatments, the overall 5-year survival rate for lung cancer in the US remains at a dismal 15.6% (Jemel et al., 2011).The situation globally is even worse, with the 5-year survival rate in China and developing countries estimated at only 8.9% (Jemel et al., 2011).

As early as 1964, a landmark report from the US Surgeon General stated the effects of smoking on health (US Department of Health and Human Services, 2010), and was recently updated in 2010 (USDHHS). There were two main findings in the report. First, cigarette smoking was associated with significant increases in the age-specific death of men, and a lower but still significant increase in the age-specific death of women. Second, cigarette smoking was causally related to lung cancer. The magnitude of the effect of cigarette smoking far outweighed all other factors causing lung cancer.

The relative risk of lung cancer caused by smoking has been found to be associated with the duration of smoking (Flanders, Lally, Zhu, Henley, & Thun, 2003; Knoke, Shanks, Vaughn, & Thun, Burns, 2004), smoking intensity (Flanders et al., 2003; Gandini, Botteri, Iodice, Boniol, Lowenfels, & Maisonneuve, 2008; Knoke et al., 2004; Mucha, Stephenson, Morandi, & Dirani, 2006), age (Flanders et al., 2003; Knoke et al., 2004), gender (Kiyohara, & Ohno, 2010), and histological types of lung cancer (Khuder, 2001; Pesch, Kendzia, Gustavsson, Jöckel, Johnen, & Pohlabeln, 2011).

The relative risk of lung cancer varies by level of smoking with respect to heavy, medium, and light smokers (Mucha et al., 2006), and when smoking is measured as a continuous variable (Gandini et al., 2008). A meta-analysis conducted by Mucha and his colleagues (2006) found that smokers who smoked less than 20 cigarettes per day had 1.44 to 1.72 times the relative risk of having lung cancer compared to non-smokers. In contrast, smokers who smoked more than 20 cigarettes per day had 1.95 to 2.75 times the relative risk of having lung cancer compared to non-smokers. Overall, the risk of lung cancer increases by 7% for each additional cigarette smoked per day (Gandini et al., 2008). There is other evidence indicating that the duration of smoking/years of cigarette smoking is an even more important factor than daily cigarette consumption in predicting lung cancer risk (Flanders et al., 2003; Knoke et al., 2004). For smokers who had an equivalent duration and intensity of smoking, the estimated absolute risk of lung cancer was higher for older smokers than for younger smokers, reflecting an increased lung cancer risk with age (Flanders et al., 2003; Knoke et al., 2004).

Findings regarding gender differences in the relative risk of lung cancer have been inconsistent. Although there are many studies suggesting female smokers have a higher risk of lung cancer relative to male smokers (Mucha et al., 2006), there are other studies reporting no measurable excess risk among female smokers compared to male smokers (Jemal, Travis, Tarone, Travis, & Devesa, 2003; Kreuzer, Boffetta, & Whitley, 2000). However, research evidence suggests women may be more susceptible to the molecular aberrations caused by smoking (Ahrendt, Decker, & Alawi, 2001; Shigematsu, Lin, & Takahashi, 2005). In addition, once female smokers developed lung cancer, DNA repair capacity was found to be lower in female lung cancer patients than in their male counterparts (Kiyohara et al., 2010). Female sex hormones may also increase susceptibility to lung carcinogenesis among female smokers (Kiyohara et al., 2010). The biological and genetic evidence lend strong support to a higher relative risk of lung cancer among female smokers. The studies reporting no differences in relative risk of lung cancer among female smokers may be due to the sample recruitment and study design.

Besides smoking intensity, duration of smoking, and gender, relative risk of lung cancer is also closely related to subtypes of lung cancer (Khuder, 2001; Pesch et al., 2011). There are three major types of lung cancer. Squamous cell carcinoma (SqCC) is the major subtype lung cancer most commonly seen in men; adenocarcinoma (AdCa) is the most common subtype observed in women; and small cell lung carcinoma (SCLC) is the one subtype affecting both genders equally (Devesa, Bray, Vizcaino, & Parkin, 2005; Govindan, Page, Morgensztern, Read, Tierney, & Vlahiotis, 2006). The relative risks differ greatly by histological type in smokers. The relative risks have been estimated from pooled analyses in Europe and Canada including approximately 30,000 respondents recruited between1985 to 2005. Relative risks were reported as 45.6 for SqCC, 45.7 for SCLC and 10.8 for AdCa (Pesch et al., 2011). Another earlier meta-analysis study reported overall lower but consistent results of 42.0 for SCLC, 25.4 for SqCC and 6.18 for AdCa among current smokers (Khuder, 2001). Although within each subtype of lung cancer the relative risks vary by gender, smoking intensity and smoking duration, the overall pattern by lung cancer subtype is consistently observed across studies (Khuder, 2001; Pesch et al., 2011).

Overall, the causal effect of smoking on lung cancer has been well-established, and the relative risks of lung cancer caused by smoking are associated with various factors including age, gender, smoking intensity, duration of smoking as well as the subtypes of lung cancer. Given the associated factors among smokers are time-specific and context-sensitive; adopting estimates of relative risk of lung cancer by smoking from other contexts requires sufficient care.

Another possible issue to consider is how a study design may lead to the great variation of relative risks reported across studies, in addition to the “real difference” caused by investigated factors. It has been reported that the definition of “smoking” has a strong impact on relative risk estimates (Simonato, Agudo, Ahrens, Benhamou, Benhamou, & Boffetta, 2001; Villanueva, Silverman, Malats, Tardon, Garcia-Closas, & Serra, 2009), especially in regards to the identification of non-smokers, a key part of reference category for estimating relative risks. Hence, the context of relative risk estimates has to be examined carefully when being adopted in other studies and research.

1.1.4 Lung Cancer and Smoking in China

With the global smoking epidemic shifting from developed countries to developing countries, one of the major consequences is that the smoking-attributable disease burden has also shifted to developing countries. In China, cancer has become a major threat to public health. Cancer mortality in China has been increasing rapidly during the past decades, from 74.2 cancer cases per 100,000 deaths in the 1970s to 108.3 per 100,000 deaths in the 1990s and to 135.9 per 100,000 deaths in 2004-2005 (China Ministry of Health, 2008; Li, Lu, Zhang, Mu, Sun, & Huangpu, 1997; National Office for Cancer Prevention and Control of the Chinese Ministry of Health, 1979). A total of 2.1 million cancer cases were estimated for the year 2000 (1.3 million in men and 0.8 million in women), with the most common sites being lung, liver and stomach cancer in men, and breast, lung and stomach cancer in women (Yang et al., 2005). In China, lung cancer has increased 465% during the past 30 years, and became the leading cancer death cause in the current decade (National Office for Cancer Prevention and Control, 2010). According to the 2008 National Health Service Survey China (Yang, Sung, Mao, Hu, & Rao, 2010), a total of 552,280 deaths in China were attributed to smoking, accounting for 8.9% of total deaths in China. Among all the smoking-attributable deaths, a total of 62% of deaths were due to cancer, followed by heart disease (27%) and respiratory disease (11%) (Yang et al., 2010).

Several studies have been conducted to estimate the burden of smoking-related cancer in China. Previous findings from a prospective cohort study (Niu, Yang, & Chen, 1998) in China indicated that tobacco was responsible for about 16% of cancer deaths in men in 1990. A more recent prospective cohort study conducted by Gu et al. (2009) found that total cancer deaths caused by smoking increased to 28.0% in men and 5.7% in women in China in 2005. Wang et al. (2010) reported smoking was responsible for 32.7% of all cancer deaths among Chinese males, and 5.0% among Chinese females in 2005. Recent evidence (Wang, Jiang, Wei, Yang, Qiao, & Boffetta, 2010) suggests that smoking accounted for 29.8% of all cancer deaths in China in 2005, and second-hand smoking has caused 1.8% of all cancer deaths in China. Overall, these findings show a clear increasing pattern of smoking-attributable cancer mortality in China, with males bearing much more cancer disease burden than females.

Differences in the smoking-attributable disease burden of lung cancer between males and females in China reflect differences in the prevalence of smoking. Smoking prevalence is as high as 66% among males and as low as 4% among female in China; thus, smoking-attributable lung cancer affects mainly Chinese males. It is estimated that smoking-attributable lung cancer is 75% (Wang et al., 2010), 50.6% (Gu, Kelly, & Wu, 2009), 52.3% (Liu, Peto, & Chen, 1998) among males in China, and 18.4% (Wang et al., 2010), 14.8% (Gu et al., 2009), 19.4% (Liu et al., 1998) among females in China. A combined analysis of 15 Chinese case-control studies reported population-attributable risks of lung cancer at 57% for males and 33% for females (Yu, & Zhao, 1996). The available recent evidence suggests that smoking-attributable lung cancer deaths in China were approximately 0.15 million in 2005, of which 0.13 million deaths were caused by active smoking (Gu et al., 2009), with another 0.02 million deaths from second-hand smoking (Gan, Smith, Hammond, & Hu, 2007).

As shown by Equation 1 below, generally speaking, the calculation of population attributable risk, or population attributable fraction, involves two key indicators (Eide, & Heuch, 2001; Ezzati, & Lopez, 2004): the relative risk of lung cancer and the smoking prevalence.

$$PAF= (P(RR-1))/(P(RR-1)+1) \quad \text{(Equation 1)}$$

Therefore, the variation in the results of population attributable risks based on available research is due to the different values used for these two indicators. Overall, the two main relative risks used across studies are mortality (death) risks and incidence (new case) risks of lung cancer. Although the difference between mortality relative risks and incidence risks were small and not significant (Yu et al., 1996), they still make a difference on the results of population attributable risks. In addition, the variation of relative risks may be the result of different definitions of smoking status.

Due to different social and living contexts in China, the relative risks of lung cancer caused by smoking in China are different from that in developed countries. Appendix B shows the summary of the major research evidence on relative risk of lung cancer caused by smoking in China. Several studies have documented the risk of lung cancer from smoking in China (Liu et al., 1998; Fu, & Gou, 1984; Hu, Galeone, Lui, Pelucchi, La Vecchia,& Negri, 2005; Gao, Blot, & Zheng, 1988; Chen, Xu, & Collins, 1997; Xu, Blot,& Xiao, 1989; Yu et al., 1996; Liu, Ho, & Huang,1990). In order to accurately investigate the overall pattern of smoking-attributable lung cancer relative risk in China, only meta-analyses and large-scale surveys of representative samples of China were examined. Local studies conducted within small samples and clinical studies are excluded.

Available evidence suggests a unique pattern of relative risks of lung cancer caused by smoking in China. First of all, the lung cancer relative risks in China are lower compared to Western countries, where the relative risks of lung cancer from smoking are as high as 10-15 times (US

Department of Health and Human Services, 2004). In a meta-analysis, Yu and Zhao (1996) found an odds ratio of 3.01 (CI: 2.64-3.46) for male smokers and 2.32 (CI 2.02-2.66) for female smokers compared with non-smokers. Liu (1998) and Liu (1992) reported similar findings, with RR values of 2.72 (CI: 2.62-2.82) and 3.09 (2.61-3.66) for men, and 2.64 (CI: 2.48-2.80) and 2.30 (CI: 1.96-2.96) for women, respectively.

The much lower risks in China might be due to two reasons. First, on average, smokers in China smoked approximately 13 cigarettes per day in 1984 and 15 per day in 1996, which is much lower than historical rates in Western countries. For example, the average daily cigarette consumption among smokers was about 30 in US in 1970 (Zang, & Wynder, 1998). Second, coal and biomass have been commonly used sources of heating and cooking fuel in the latter half of the last century in China. Air pollutants from these sources may increase the background lung cancer rate among non-smokers, resulting in overall lower relative risk of lung cancer among smokers.

Second, in contrast to higher relative risks of lung cancer among female smokers in Western countries, Chinese male smokers had a higher relative risk of lung cancer (Gu et al., 2009; Liu, 1992; Liu et al., 1998; Jiang, Liu, Nasca, Chen, Zeng, & Wu, 2008; Yu et al., 1996); however, when further examined by daily cigarette consumption, relative risks for female for each daily cigarette consumption category were consistently higher than their male smoker counterparts within same daily cigarette consumption category (Gu et al., 2009; Liu et al., 1998; Jiang et al., 2008; Yu et al., 1996). Even in the same study which investigated both overall relative risks among males and females and daily cigarette consumption among male and female separately, the patterns remained consistent. One possible reason for the higher overall relative risks and relatively lower cigarette consumption categorical relative risk for lung cancer among males in China might be the high second-hand smoking exposure among Chinese female non-smokers as a whole. Smoking prevalence in China is 57.4% among males with an average of 15 cigarettes consumed daily, and 2.6% among females with an average of 10 cigarettes consumed daily (Yang et al., 2005). The very high smoking prevalence and high daily cigarette consumption among Chinese males have resulted in a large number of non-smoking females being exposed to second-hand smoking, which has, in turn, elevated the overall "background" risk of lung cancer among non-smoking females compared with non-smoking males in China. Hence, when examining males and females separately, the elevated "background" relative risk of lung cancer among female non-smokers may have narrowed the relative risk of lung cancer among female smokers.

Third, a recent meta-analysis (Nakamura, Huxley, Ansary-Moghaddam, & Woodward, 2009) suggests the relative risk for smoking- attributable lung cancer among current smokers (compared to never smokers) in China was 2.78 (CI: 1.63 to 4.75). Former smokers had reduced relative risks compared to current smokers for lung cancer of 1.96 (CI: 1.38 to 2.79). In contrast to the reduced risk after quitting among smokers in developed countries, quitting in China provides a relatively minor reduction in relative risk of lung cancer. In the same study, Nakamura et al. (2009) even found an increased risk for respiratory disease after quitting among smokers in China. One of the possible reasons for the benefits of quitting being less apparent in China might be a difference in quitting behaviour. There is some evidence to suggest that the reasons for quitting smoking differ considerably between developed and developing countries. In developed countries, smokers are more likely to quit due to anticipating harmful health effects of smoking (Romer, & Jamieson, 2001). In China, where the hazards of smoking are much less widely known, the primary reason for quitting is smokers actually getting sick (Qian et al., 2009; Yang et al., 2001). Consequently, the beneficial effects of smoking cessation are less likely to be experienced among Chinese smokers who may be quitting only once smoking-attributable diseases manifest (Doll et al., 2004; Huxley et al., 2007). Therefore, the current pattern of quitting smoking and associated unique relative risks of smoking-attributable diseases strongly suggest an urgent need to promote smoking cessation in China. Due to the long latency period between smoking and onset of smoking-attributable diseases, smoking-attributable disease burden is still relative low in China. Effective smoking cessation will be essential to help China to avoid smoking-related disease burden in the upcoming several decades.

Fourth, similar to research from Western countries, available evidence in China suggests the relative risks of lung cancer is associated with increased daily cigarette consumption and longer smoking duration (Gu et al., 2009; Liu, 1992; Liu et al., 1998; Jiang et al., 2008; Yu et al., 1996). Research on the relative risk of subtypes of lung cancer caused by smoking is limited in China, but existing findings indicated that the most common type of squamous lung cancer had much higher relative risk (4.75) than non-smokers. The absolute value of relative risk of squamous lung cancer among smokers is much lower than that found in Western countries (relative risk of 45.6); however, given the overall lower relative risk of lung cancer among Chinese smokers, the general pattern is consistent with that of Western countries.

1.1.5 Urban and Rural China

In China, the mortality of cancer is higher in urban areas (e.g., 150.18 cases per 100,000 people) than in rural areas (e.g., 128.65 cases per 100,000 people). In urban areas, lung cancer is the leading cancer followed by digestive tract cancers, such as liver cancer, esophageal cancer and colorectal cancer. In contrast, in rural areas, liver cancer is most common, followed by lung cancer and other digestive tract cancers (Zhao, Dai, Chen, & Li, 2010).

In China, urban and rural areas have significant differences in smoking prevalence as well as smoking-attributable disease patterns and healthcare operation systems. With higher smoking prevalence among males in rural areas relative to urban China (56.1% vs. 49.6%), the female smoking prevalence in rural areas is lower than their counterparts in urban areas (2.2% vs. 2.6%). Different smoking prevalence rates together with different living environments consequently have resulted in different relative risks of various smoking-attributable diseases as well as disease burden. Overall, the relative risk of lung cancer among female smokers is higher in urban areas (female vs. male= 3.24 vs.2.98), while in rural areas, the pattern shows the opposite (female vs. male= 1.98 vs. 2.57). Existing evidence has indicated that the relative risks from lung cancer among male smokers were consistently higher in urban than in rural areas across light, medium and heavy smokers (Liu et al., 1998).

1.1.6 Smoking and Its Economic Effects in China

The low smoking cessation rate and upcoming peak of smoking-attributable disease burden are closely associated with China’s unique social and economic context for the tobacco industry. The unique economic role the tobacco industry plays in China makes tobacco control not a merely public health issue, but also an economic issue, which to a certain extent has hampered tobacco control in China.

In China, tobacco marketing and even the tobacco leaf supply are being charged by the China National Tobacco Company (CNTC), which is managed by a government department known as China the State Tobacco Monopoly Administration (STMA). Therefore, in China, everything from tobacco leaf planting to the retail sales of cigarettes is under total control by the Chinese government. As a government-owned monopoly, the Chinese government not only benefits from the taxes of the tobacco leaf provided by local government, but they also profit from the tobacco retail by CNTC. The tobacco industry in China appears to be the top contributor to government by providing 7 to 11 percent of its revenue (profit and tax) over the past 15 years (Liu, & Xiong, 2004). Figure 2 shows the tax and profit revenue contributed by the tobacco industry in China from 1996 to 2003. According to the figure, in 2003, CNTC generated $2 billion US dollars, accounting for 7.4% of government revenue (Liu et al., 2004). In 2005, cigarette sales in China generated $32.5 billion in taxes and profits, approximately 7.6% of the government's total revenue (Wright, & Katz, 2007). In some of China's "big tobacco" provinces, such as Yunnan province, the profits and tax from tobacco accounted for 50% of government revenue (Wright et al., 2007).

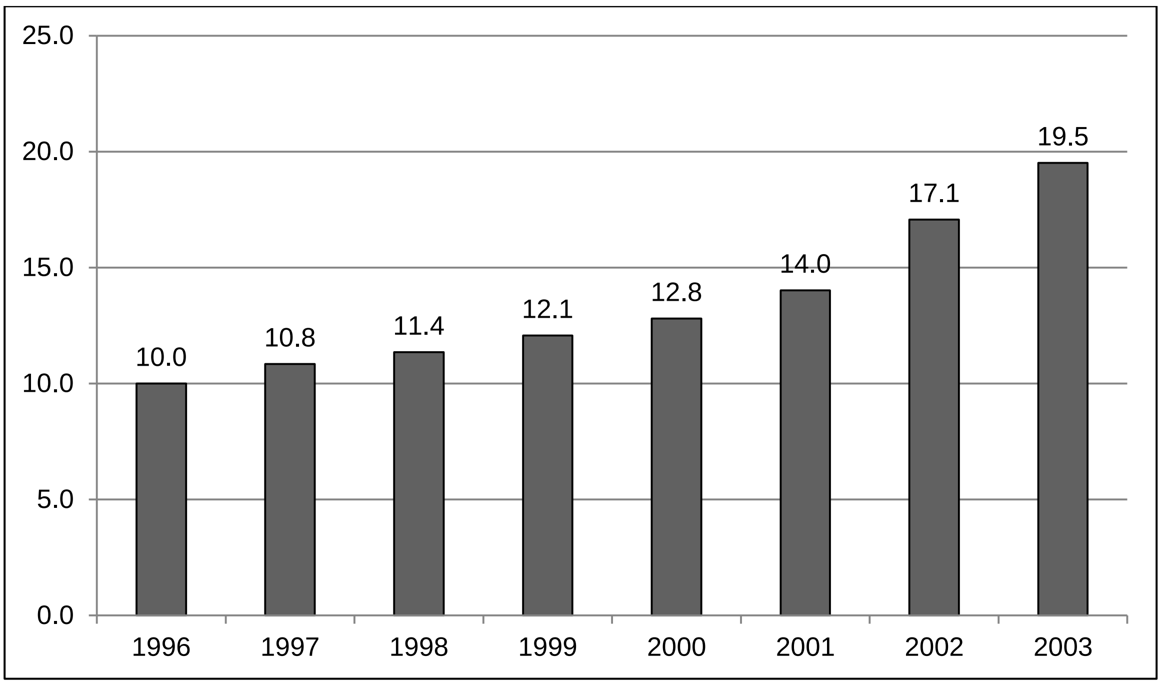


Figure 1.2: Tax and Profit Revenue Contributed by Tobacco Industry in China (in U.S. billion)

Sources: Liu T, and Xiong B. Tobacco Economy and Tobacco Control (in Chinese), Beijing, China: Economic Science Press, 2004:169.

With an annual production of 1.7 trillion cigarettes a year on average, or roughly one third of the world's total supply, CNTC provides a great amount of employment opportunities in China. An estimated 4 million Chinese households rely on tobacco for their livelihood, either as tobacco farmers, cigarette industry employees, or cigarette retailers (Liu et al., 2004). Therefore, for the Chinese government, the tobacco industry has been considered as an important component to economic growth (Wright et al., 2007). With the significant tax and profit revenues as well as employment opportunities provided by tobacco industry, the Chinese government has become concerned about the negative economic consequences resulting from tobacco control measures.

However, with the cost caused by smoking-attributable disease increasing significantly and quickly in recent years, China is at a crossroads between tobacco control and economic benefit from tobacco industry. Figure 3 shows the pattern of the cost of smoking in China. Available evidence has suggested a rapid increase in the cost of smoking-attributable disease burden. An earlier study (Jin, Lu, Yan, Fu, Jiang, & Li, 1995) estimates the economic cost of smoking in China in 1989 was $3.27 billion (at the exchange rate of U8.2784 to US$1 in 1989), including $0.83 billion of direct medical costs and $2.43 billion of indirect morbidity and mortality costs. Sung et al. (2006) estimated the 2000 economic cost of smoking in China was $5.0 billion (at the exchange rate of U8.2784 to US$1 in 2000), of which $1.7 billion were direct medical costs of smoking and $3.3 billion were indirect morbidity and mortality costs. Furthermore, the direct medical cost of smoking accounted for 3.1% of China's national health expenditures in 2000 (Sung, Wang, Jin, Hu, & Jiang, 2006). The most recent study by Yang and Sung and there colleages (2010) estimated the smoking-attributable cost in China in 2003 and 2008, respectively. The findings reported that the total economic cost of smoking in China amounted to $17.1 billion in 2003 and $28.9 billion in 2008 (both measured in 2008 constant US$). Direct smoking-attributable medical costs in 2003 and 2008 were $4.2 billion and $6.2 billion, respectively (Yang et al., 2010). Indirect economic costs, including the cost of transportation, nutritious supplemental food and caregiver costs during inpatient hospitalisations and outpatient visits due to treating smoking-related diseases, and lost productivity costs caused by smoking-related illness, in 2003 and 2008 were $12.9 billion and $22.7 billion, respectively (Yang et al., 2010). Comparing the cost of smoking in 2003 and 2008 to 2000, the direct costs of smoking rose by 72% in 2003 and 154% in 2008, while the indirect costs of smoking rose by 170% in 2003 and 376% in 2008 (Yang et al., 2010).

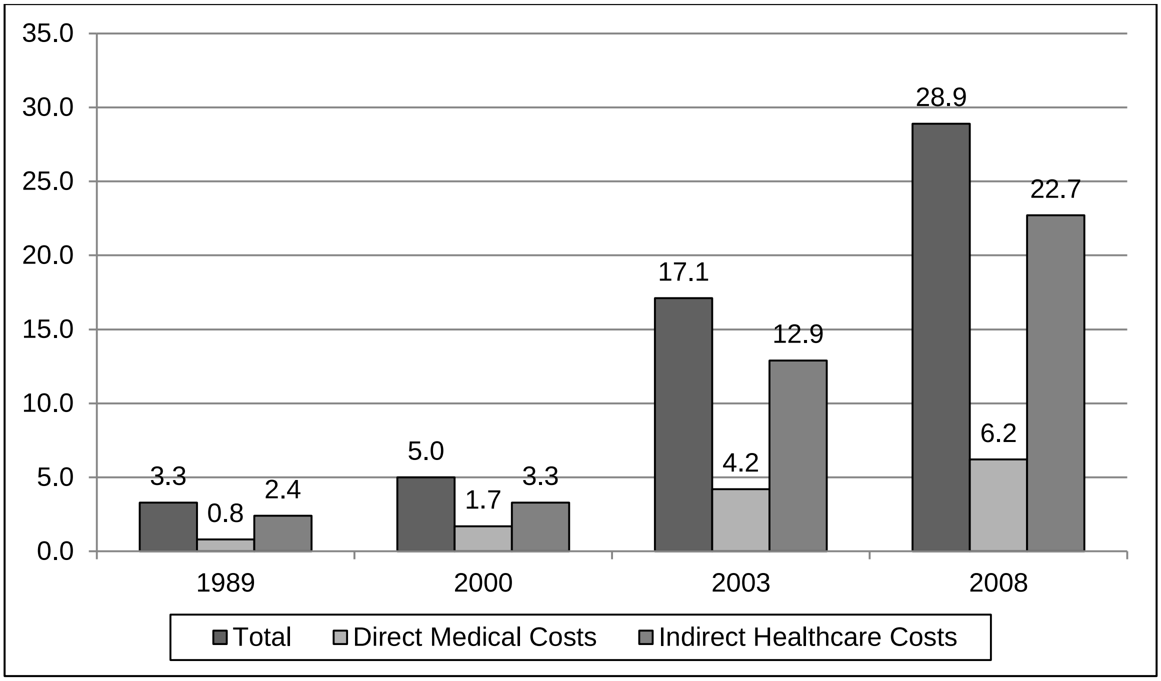


Figure 1.3: Smoking-Attributable Cost 1989-2008 in China (in U.S. billion)

Figure 3 suggests a clear and fast increasing pattern of smoking-attributable disease burden in China. In 2008, the cost of smoking in China was close to 10 times to the cost in 1989 (not adjusted for inflation). The indirect health care cost is also much greater than the direct medical cost of smoking in China. Smoking costs to the Chinese society is rising much faster than the increased revenue brought by tobacco industry. It is worth mentioning that the calculation of cost based on available evidence may be a partial reflection of the smoking cost since only estimated the costs of major smoking-attributable disease, such as lung cancer, respiratory disease, and heart disease are included; the large amount of other smoking-attributable diseases, such as dental disease and breast cancer, are not included due to limited data. Furthermore, the cost caused by second-hand smoking has not been estimated in China. Given that the majority of non-smokers in China are exposed in second-hand smoke (Yang et al., 2005), the disease burden and cost of smoking cannot be ignored. Therefore, the actual cost of smoking to Chinese society is much more than the existing evidence suggests. The economic benefits generated by tobacco industry are greatly challenged by the cost of smoking in China. Tobacco control is urgently needed in China from both public health and economic perspectives.

Understanding the unique economic priorities and the tobacco industry situation in China can help identify effective solutions for tobacco control. China is not only home to one third of smokers in the world, but more importantly, there are even more non-smokers in China affected by second-hand smoking, among which the smoking disease burden and costs are estimated to be substantially high. Hence, tobacco control in China is important for global efforts to reduce the smoking-attributable disease burden.

1.2 The Healthcare System and Smoking Cessation

1.2.1 Overview

Currently, there is no smoking cessation intervention widely implemented in the healthcare system of China. In Western countries, smoking cessation interventions have been broadly promoted in clinical settings either in behaviour counselling or medical treatment, or the combination of both. A systematic review for each approach concludes that all are effective at increasing the smoking cessation rate through behavioural change, nicotine dependence treatment, or both (Eisenberg, Filion, Yavin, Bélisle, Mottillo, & Joseph, 2008; Gainsbury, & Blaszczynski, 2011; Mottillo, Filion, Bélisle, Joseph, Gervais, & O'Loughlin, 2009; Shahab, & McEwen, 2009; Stead, Perera, & Lancaster, 2007; Wu, Wilson, Dimoulas, & Mills, 2006).

There is increasing evidence suggesting healthcare systems play an important role in successful smoking cessation (Curry, Keller, Orleans, & Fiore, 2008). First, healthcare systems provide an opportune setting not only to contact and intervene with smoking patients, but also to broaden the reach of effective smoking cessation treatments (Hovell, Roussos, Hill, Johnson, Squier, & Gyenes, 2004; Shroeder, 2005). In developed countries, an estimated 70 to 80% of adult smokers visit physicians annually (Curry, Sporer, Pugach, Campbell, & Emery, 2007; Curry et al., 2008; Fiore, Jaén, Baker, Bailey, Bennett, & Benowitz, 2008). In China, recent evidence suggests only one-third of smokers visit their doctors each year (Yang et al., 2010). Given that China is still in the early stages of the smoking epidemic, with an increasing smoking-attributable disease burden in China, it is expected that a higher proportion of Chinese smokers will appear in the healthcare system over time. Thus, the healthcare system may serve as a potentially useful setting to reach smoking patients in the future. Another reason that gives evidence to the utility of healthcare systems in smoking cessation is that patients usually regard doctors as credible and reliable authorities in health issues, and generally adhere to physicians' health advice (Stein, Haddock, O'Byrne, Hymowitz, & Schwab, 2000). Third, poor health is a strong motivator for smoking cessation. Finally, cigarette smoking is a chronic disease due to tobacco dependence (Fiore et al., 2008). Medical treatment is particularly important for heavy smokers who are more heavily nicotine dependent (Fiore et al., 2008).

Two well-established smoking cessation interventions provided in healthcare system in Western countries are behavioural counselling and pharmacological medication on nicotine dependence. The available behaviour counselling and medication treatments vary greatly in types of providers, length, material used, follow-up contacts and recruitment strategy; however, the efficacy is well-established across studies (Fiore et al., 2008; Stead, Bergson, & Lancaster, 2008), although the findings on effect size are not consistent due to a vast variety of intervention designs.

Evidence from Western countries has shown that even brief quitting advice from physicians significantly increases motivation to quit (Stead et al., 2008; Stein et al., 2000). Among various physician counselling interventions, the 5A's model is widely recommended, and consists of the following components: "Ask (screen for smoking), Advise (provide a quit message), Assess (evaluate readiness to quit), Assist (provide treatment), and Arrange (track cessation progress)" (Fiore, 2000). NRT is the most popular pharmacological medication for smoking cessation, among which nicotine patch is the most often used NRT products. Robust evidence has demonstrated that smoking patients receiving pharmacotherapy are approximately 1.5 to 2.0 times more likely to remain abstinent (for over 6 months) compared with patients receiving placebo (Stead et al., 2008). Based on the strong available evidence, it has been recommended in Clinician Practice Guidelines in the U.S. (Fiore et al., 2008) that every smoking patient should be offered at least the brief advice on smoking cessation and all smoking patients should be encouraged to quit by using both counselling and medication.

In Western countries, the available supporting evidence on implementation of smoking cessation interventions in healthcare system is not only on effectiveness, but also cost-effectiveness. Economic evaluation, increasingly used in recent years, assesses the effectiveness of the health outcome of health care interventions by economic terms, or value for money, to help identify those effective interventions that cost the fewest resources – so called "cost-effective" (Drummond, Sculpher, Torrance, O'Brien, & Stoddart, 2005). Since 1990's, the economic cost of health care interventions has been progressively acknowledged as an important factor for a stakeholder to decide their availability. In the case of smoking cessation interventions, economic evaluation provides the evidence on cost per unit measure of effectiveness of these interventions, such as cost per quitter or cost per life year saved. This allows stakeholders to make straightforward comparisons either between smoking cessation interventions or across different health care interventions. Existing economic evidence from Western countries indicates that various smoking cessation interventions, such as physician counselling and NRT, are not only effective, but also highly cost-effective compared to other preventive interventions based on selected smoking- attributable disease (Cornuz, Gilbert, Pinget, McDonald, & Slama, 2003; Kahende, Loomis, Adhikari, & Marshall, 2009; Warner, 1997).

Unfortunately, in middle and low income countries that are home to a total of 80% of worldwide smokers (WHO, 2008), there is limited research evidence on the effectiveness and cost-effectiveness on smoking cessation intervention in healthcare systems. Given the upcoming high smoking-attributable disease burden as well as a relatively tight health care budget, the evidence on effectiveness and cost-effectiveness is particularly important for middle and low income countries to formulate optimal smoking cessation programs.

As previously mentioned, the tobacco industry in China is state-owned and has generated 7 to 11% of government revenue in past 15 years (Liu et al., 2004); this makes tobacco control not only a public health issue, but also an economic issue. With clear economic benefits gained from the tobacco industry, economic evaluation on smoking cessation interventions is urgently needed in order for the Chinese government to better allocate resources to protect public health.

1.2.2 Smoking Cessation Intervention Delivery in Healthcare Systems

Besides the design of smoking cessation interventions, the delivery of the programs is also strongly associated with their effectiveness. Briefly speaking, the factors from physician, patients, and health system structures together affect the delivery of smoking cessation interventions in a healthcare system. In Western countries, it is estimated that about 40 to 70% of physicians have provided smoking cessation advice to their smoking patients (CTUMS, 2006; Longo, Stone, & Phillips, 2006). Since developing countries are in the early stages of smoking cessation, the provision of smoking cessation aids by physicians in the healthcare system is lower in China. Studies have shown that approximately 20 to 50% of Chinese physicians gave specific smoking cessation assistance to their smoking patients, including counselling, self-help materials, quit-smoking medications, or follow-up support (Cui, Lu, & Chen, 2007; Jiang et al., 2007; Young, & Ward, 2001).

In clinical settings, the physician plays a critical role in the effectiveness of cessation interventions. Physicians on the front-line provide interventions either by prescription management or counselling and are responsible for determining the best cessation approach for each patient and the length of each intervention. Individualized medical prescriptions and quitting advice greatly affect cessation outcome (Bars, Banauch, & Appel, 2006). Previous research suggests that physicians' smoking status significantly affects their provision of smoking cessation advice. Furthermore, physicians who have a positive attitude toward smoking cessation (Vogt, Hall, & Marteau, 2005) and those with better personal health habits (Meshefedjian, Gervais, Tremblay, Villeneuve, & O'Loughlin, 2010) are more likely to effectively deliver a smoking cessation intervention. In addition, female physicians (Barengo, Sandstrom, Jormanainen, & Myllykangas, 2005; Squier, Hesli, Lowe, Ponamorenko, & Medvedovskaya, 2006) and non-smoking physicians (Meshefedjian et al., 2010; Sotiropoulos, Gikas, & Spanou, 2007) were more likely to advise their smoking patients to quit. Physicians who received training on smoking cessation had higher engagement levels in assisting patients to quit smoking (Stead, Angus, Holme, Cohen, & Tait, 2009; Twardella, & Brenner, 2005). The physicians who reported low perception of effects, shortage of time, lack of delivery skill, reluctance to raise the issue of smoking due to its sensitivity, and perception of low motivation by patients were less likely to initiate smoking cessation intervention during patient visits (Richmond, & Anderson, 1994; Young et al., 2001).

Patient characteristics also have an influence on physicians' provision of smoking cessation interventions. Generally, physicians are more likely to give cessation advice to patients who show smoking-attributable disease (Kossler, Lanzenberger, & Zwick, 2002), are heavy smokers (Devroey, Kartounian, & Vandevoorde, 2004; Hoch, Muehlig, & Höffler, 2004), or are pregnant (Windsor, Oncken, Henningfield, Hartmann, & Edwards, 2000).

Cost is a potential barrier to the use of cessation interventions. Besides the factors associated with physician and smoking patients, the structural factor of patients' reimbursement status is also important during the delivery of smoking cessation intervention in the healthcare system. Research evidence shows that a lack of reimbursement was a significant reason cited by a physician for not providing a smoking cessation intervention to their smoking patient (Brotons, Bjorkelund, Bulc, Ciurana, Godycki-Cwirko, & Jurgova, 2005; Hannover, Thyrian, & John, 2004).

The low provision of smoking cessation interventions might be explained by several reasons. First, smoking prevalence among Chinese physicians is high. Studies indicate that the overall smoking prevalence among Chinese physicians was 20 to 23%, among which male physician smoking prevalence was 41 to 54% (Jiang et al., 2007; Wu, & Min, 2007). Second, the overall low health knowledge on smoking among Chinese physicians may be a further limitation to providing cessation advice. For instance, only an estimated two-thirds to one-half of Chinese physicians know that active and passive smoking could cause lung cancer (Jiang et al., 2007). Last and most importantly, Chinese physicians may be less likely to provide smoking cessation counselling due to limited training. Research has found that only 10% of Chinese physicians ever received training on smoking cessation counselling (Jiang et al., 2007), but physicians who received training on smoking cessation were more likely to give quit advice to patients (Lam, Jiang, Chan, & Chan, 2011), a finding consistent with the pattern in Western countries.

Considering the overall early stage of the smoking epidemic in China featured high smoking prevalence and low smoking cessation, the currently low rate of physician visits for smokers is a strong indicator of the upcoming peak of smoking-attributable disease burden in China. The lower proportion of smokers visiting a doctor demonstrates the urgent need for implementation of smoking cessation interventions in the healthcare system to avoid a high smoking-attributable disease burden in the future. In order to introduce smoking cessation interventions into China's healthcare system, there is a need to better understand the effectiveness of such interventions; insight may be acquired by using the evidence from Western countries and by identifying unique factors affecting delivery in China.

1.3 Effectiveness of Physician Counselling and NRT for Smoking Cessation

1.3.1 Physician Counselling

As early as the 1980s, it was observed that advice from physicians to their smoking patients was effective in facilitating smoking cessation (Cohen, Stooky, Katz, Drook, Smith, 1989; Kottke, Brekke, Solberg, & Hughes, 1989; Kozlowski, & Page, 1987). In the 1990s, physician counselling was officially recommended in the Smoking Cessation Guidelines for Health Professionals (West, McNeill, & Raw, 2000), strengthening periodically in Western countries (Fiore et al., 2008).

From a smoking cessation perspective, smoking patients who visit the healthcare system may be categorized into one of two groups: willing to quit or unwilling to quit. Recommending a patient who is unwilling to quit smoking to enter a smoking cessation program is apparently premature and will most likely be ineffective. Any intervention efforts will not be successful unless smoking patients are sufficiently motivated to quit smoking. Therefore, when smoking patients enter into the healthcare system, identifying their intention to quit is the first priority.

The provision of smoking cessation interventions to both groups of willing and unwilling to quit can be done using different strategies (Fiore, 2000). For smokers who are unwilling or not ready to quit, the U.S. practice guidelines suggest following the ‘‘5 R’s’’ for motivational intervention: Relevance, Risks, Rewards, Roadblocks, and Repetition. During this intervention, a smoking patient should be asked to: 1) identify why quitting smoking is personally relevant to the patient (e.g., how smoking associated with patient’s own health; health of patient’s children); 2) identify potentially negative consequences, or risks, of tobacco use (e.g., cancer; respiratory disease, and cardiovascular problems and cancer, the risks to children of breathing second-hand smoke; as well as increased risks of their children becoming smokers); 3) identify rewards associated with cessation (e.g., reduced smoking-attributable risks, financial savings); 4) identify roadblocks or barriers to quitting and note treatment elements that could address them (e.g., withdrawal symptoms, such as appetite increase, risk of depression, weight gain); and, 5) the doctor should repeat the above information every time the patient visits the healthcare system.

For those identified as “willing” to quit smoking, it is recommended that a physician performs brief counselling based on the 5A model – Ask, Advise, Assess, Assist, and Arrange. Within this intervention, a smoking patient should be: 1) asked about smoking at his every healthcare system visit; 2) advised to quit; 3) assessed for the quit intention; 4) assisted with strategies for quitting; and, 5) arranged for follow-up contacts.

For the smokers who are willing to quit, the 5A model is actually one of the more standardized brief counselling intervention types. Across the existing physician counselling interventions, there is currently no standard definition or suggested format. Physician advice on quitting can be delivered to patients in either as brief as 30 seconds by one physician in one visit, or more intensive counselling involving one of more components of additional advice from a physician or nurse, referral to a cessation clinic, follow-up visits, and provision of smoking cessation manuals (Stead et al., 2008).

The efficacy of physician counselling has been well-researched in Western countries. Despite the varied forms of physician counselling, a recent meta-analysis found that compared to no advice, either brief or intensive counselling yields significant increases in quit rates (Fiore et al., 2008). Motivational interviewing is effective by triggering smokers’ quit attempts (RR = 1.27, CI = 1.14–1.42) (Lai, Cahill, Qin, & Tang, 2010). Even a 3-minute physician counselling session can significantly increase the smoking cessation rate (OR=1.3) relative to no counselling (Fiore et al., 2008). Findings from the USDHHS Clinical Practice Guidelines show that brief physician advice (i.e., 2 to 5 minutes) was associated with a higher chance of smoking cessation (OR 1.3, 95% CI 1.1–1.6) (Fiore et al., 2008). A Cochrane review of 17 studies found a similar finding indicating that smoking patients who received brief physician advice were more likely to quit smoking than those not receiving any quitting advice (OR=1.66, CI=1.42–1.94) (Stead et al., 2008).

There is a strong dose-response relationship between the intensity of tobacco dependence counselling (both duration for each counselling session and total number of counseling sessions and its effectiveness). According to a recent meta-analysis of 35 randomized trials (Fiore et al., 2008), quit rates increased significantly with minutes of total counseling contact. Compared with the 11% quit rate for the no counselling group, the quit rate increased to approximately 14% for the group that received 1 to 3 minutes of brief counseling, 19% for 4 to 30 minutes of counseling, and 27% for 31 to 90 of intensive counseling. Evidence from earlier meta-analyses also confirmed the positive association between quit rate and intensity of cessation counselling (USDHHS, 1996; Rennard, & Daughton , 2000). In another recent review (Stead et al., 2008), evidence suggested that, when compared with no counselling group, the intensive physician counselling has higher effect of increasing quit rate (RR=1.84, 95% CI=1.60-2.13) than brief counselling (RR=1.66, 95%, CI=1.42 to 1.94). Direct comparison of intensive versus brief advice also indicated a significant advantage of intensive advice (RR 1.37, 95% CI=1.20 to 1.56).

The efficacy of quitting counselling in healthcare system was also evaluated from other perspectives, including provision by physician vs. non-physician, and group counseling vs. individual counselling. A review of 29 studies by Fiore and colleagues (2000) found counselling provided by non-physicians significantly increased quit rate (OR 1.7, CI 1.3–2.1), and among different providers, there is no specific clinician type which demonstrated superiority. Group therapy and individual counseling are the most effective types of treatment and are equally effective (Lancaster, & Stead 2005; Stead, & Lancaster, 2005;).

1.3.2 NRT

NRT is the most frequently used stop-smoking medication. NRT partially replaces the nicotine from cigarettes over the initial weeks after stopping smoking. Currently, there are a total of five types of NRT widely available in the market, including nicotine gum, nicotine patches, nicotine spray, nicotine inhaler, and nicotine lozenge/tablet. NRT products help to reduce tobacco physiological withdrawal symptoms during the period following smoking cessation when such symptoms are most severe, and thus increase the likelihood of remaining abstinent (Henningfield, 1995). Among the five NRT products, nicotine gum, lozenge, inhaler and spray are classified as short-acting products, while the NRT patch is categorized as a long-acting product. Appendix C shows the summary of effectiveness of various NRT products in Western countries.

Research evidence (Fiore et al., 2008) suggests that all NRT products significantly may increase the 6-month quit rate when used individually. When NRT products were used on their own, the probability to quit among smoking patients increased to 1.5 (95% CI=1.2-1.7) times for nicotine gum; 2.3 (95% CI=1.7, 3.0) for nicotine spray, 1.9 (95% CI=1.7, 2.2) for nicotine patch (Fiore, 2008). (Note: the effectiveness of nicotine lozenge/tablet was not reported in Fiore, 2008). Another recent meta-analysis found the odds ratios ranged from 1.71 (95% CI=1.35-2.21) for nicotine gum, 2.06 (95% CI=1.12- 5.13) for nicotine lozenge/tablet, 2.07 (95% CI=1.69- 2.62) for nicotine patch, to 2.37(95% CI=1.12-5.13) for nicotine spray (Eisenberg et al., 2008). The effectiveness of NRT products were further demonstrated in a study that found the odds ratios for the different forms of NRT were 1.66 (95% CI: 1.52 to 1.81) for gum, 1.81 (95% CI=1.63 to 2.02) for patches, 2.35 (95% CI=1.63 to 3.38) for nasal spray, and 2.05 (95% CI: 1.62 to 2.59) for nicotine tablet/lozenge (Silagy et al., 2007).

The effectiveness of combination use of NRT products have been inconsistently reported across studies depending on different combinations. Meta-analysis evidence suggests that nicotine patches and inhalers used together increased the quit rates by 2.2 times (95% CI=1.3- 3.6), while nicotine patch combined with nicotine gum or nicotine spray increased the quit rate by 3.6 times (95% CI=2.5-5.2) among smoking patients (Fiore, 2008). The available meta-analysis evidence on effectiveness of other NRT products combinations is limited. In a few single trials, the combination of a nicotine patch with an inhaler or spray showed non-significant increases in the quit rate (Bohadana,,Nilsson, Rasmussen, & Martinet, 2003; Croghan, Sloan, Croghan, Novotny, Hurt, & DeKrey, 2003; Tonnesen, Paoletti, Gustavsson, Russell, Saracci, & Gulsvik, 1999).

The duration of NRT treatment for smokers varies depending on the smokers' smoking history and demographic characteristics. Differences in the dosage effectiveness of NRT have emerged for light vs. heavy smokers (Fiore, 2000; Silagy, Mant, Fowler, & Lodge, 1994; Sonderskov, Olsen, Sabroe, Meillier, & Overvad, 1997). Research evidence suggests that high dose nicotine gum (4mg) was more effective among highly nicotine dependent smokers (cigarette per day >25) smokers (OR=2.2), while no effect was observed among light smokers (cigarette per day <15) (Garvey, Kinnunen, Nordstrom, Utman, & Doherty, 2000). No significant differences were apparent in terms of clinical effectiveness for 16-hour, 24-hour, high dose and standard patches, or combinations of more than one NRT use vs. using only one form of NRT alone.

The quit benefit from using NRT was most evident during the 6- to 12-months of follow up. The long-term relapse rate for former smokers was estimated as 35% after 12 months of follow up of NRT treatments; however, the relapse rate is similar to the control group, which makes the odds ratio of NRT effectiveness stable (Hughes, Keely, & Naud, 2004). Existing long-term follow-up data suggested that whether using no assistance, or with NRT or other medical assistance, approximately 30% of the subjects who have been abstinent for 1 year, will relapse some time during the following 5 years (Gilpin, Pierce, & Farkas, 1997; USDHHS, 1999). Relapse after 5 years may occur, but the rate is insignificantly low (Gilpin et al., 1997; USDHHS, 1999).

There is insufficient evidence on safety and efficacy of NRT in specific sub-populations, such as pregnant women, smokeless tobacco users, patients with psychological problem, youth; therefore, none of the NRT products are currently indicated for use in these populations (Fiore et al., 2008).

Although both pharmacotherapy and behavioural counselling are effective independently, patients' odds of quitting are substantially increased when the two approaches are used synergistically (Fiore et al., 2008). Fiore and his colleagues (2008) found the combination of counseling with medications works to increase quit rates by 1.7 times compared to counseling alone. However, the effects of the combination of the two approaches were not affected by intensity of physician counselling, which means there is no significant difference between brief physician counselling and intensive physician counselling when they are jointly offered with a certain NRT product (Silagy et al, 2007).

1.3.3 Effectiveness of Physician Counselling and NRT in China

Physician counselling and NRT are not widely promoted or routinely available in the healthcare system in China. Although physician counselling and NRT use exist, the evaluation of their effectiveness in the Chinese population is limited.

A study conducted in Hong Kong found that doctors' advice on quitting did not have any impact on patients' intentions to quit and successful quitting (Yu, Wu, Abdulla, Chai, & Chai, 2004). A recent population-based study in China found doctors' advice significantly increased the likelihood of quit attempts (OR=1.74, CI= 1.33-2.29) among Chinese smokers. However, doctors' advice was not associated with higher levels of smoking cessation (Yang et al., 2010). The existing evidence exhibited a weak impact of doctor's quitting advice on a smoker's cessation behaviour. This could be possibly explained by the limited training received by Chinese physicians. Particularly, the high smoking prevalence among Chinese physicians combined with insufficient health knowledge on smoking (Jiang et al., 2007) suggest smoking cessation training among Chinese physicians is urgently needed, and must be a priority item to include in the training of new physicians.

Compared with physician counselling, NRT is used even less often among Chinese smokers. Recent national data show only about 6% of Chinese smokers who attempted to quit used NRT (Yang et al., 2010). Although NRT is available both by prescription and over the counter in China, anecdotal evidence suggests that NRT is not widely accepted nor considered as an effective and viable smoking cessation aid among Chinese smokers. High retail price and low NRT marketing are often cited as reasons for the low prevalence of NRT use in China (Lam, Abdullah, Chan, & Hedley, 2005; Zhong, 2009). In a local study conducted in Hong Kong (Lam et al., 2005), even when NRT products were provided for free, 66% of respondents refused to use or stopped taking the therapy. Research findings indicated that the smokers who were highly educated (had college education or above), had previous experience of using NRT, and perceived tobacco to be addictive were more likely to use NRT (Lam et al., 2005). Overall, a lack of awareness and high NRT retail price are two major reasons for low NRT use in China.

Due to the low prevalence of NRT use in China, studies on the effectiveness of NRT among Chinese smokers are rare. In order to fully observe NRT use in China, a review of the existing evidence from not only randomized controlled studies conducted in clinical settings, but also the available population studies were examined (Appendix D).

There were a total of six studies currently available on NRT use among Chinese smokers, among which two were randomized controlled trials conducted in a clinical setting (Sun, Guo, Chen, Jiang, Liu, & Di, 2009; Yu, Zang, & Lin, 2006), while the others were population-based studies (Abdullah, Lam, Chan, & Hedley, 2006; Abdullah, Lam, Chan, Leung, & Chi, 2008; Lam et al., 2005;Yang et al., 2010). NRT products used across the studies included the nicotine patch, nicotine tablet, and nicotine gum. Behavioural counselling was provided adjunct to NRT in almost all studies (Abdullah et al., 2006; Abdullah et al., 2008; Lam et al., 2005; Sun et al., 2009; Yang et al., 2010). The courses of treatment ranged from 7 to 12 weeks, with abstinence rates collected at 3- to 18-month follow-up visits. Except for one population-based study (Yang et al., 2010), all existing evidence suggested NRT significantly increased the likelihood of smoking cessation among Chinese smokers. Although evidence on the effectiveness of NRT from China is comparable to the evidence from Western countries, the insufficient information on study design and respondent recruitment, as well as inconsistent reporting on the clinical NRT use from those suggested by US FDA, these findings may be biased to certain extent.

A meta-analysis based on Western countries found little evidence about the role of NRT for individuals smoking less than 10 to15 cigarettes a day (Silagy, Lancaster, Stead, Mant, & Fowler, 2007). Among the available research in China, the average cigarette daily consumption for 70% of subjects in one study was found to be less than 10 cigarettes per day (Abdullah et al., 2006), while another study estimated that approximately half of subjects smoked less than 10 cigarettes per day (Abdullah et al., 2008). However, both studies were conducted among elderly over 60 years and youth under 24 years old (Abdullah, et al., 2006; Abdullah et al., 2008), which is not representative of the general population; hence, these research findings are not applicable to the following research comparisons between Western countries and China.

Generally speaking, the short-term effectiveness of NRT was determined by a 3-month (or 12-week) smoking abstinence rate, while the long-term effectiveness was reflected at the 6- to 12-month abstinence rate. Findings on short-term effectiveness of NRT in China (Sun et al., 2009, Yu, 2006) found ORs of 1.55 and 2.18, respectively, which are comparable to the findings in Western countries, where the pooled OR of forty-one trials for 3-month sustained abstinence was 2.04 (95%CI: 1.80-2.31) (Wu et al., 2006). The lower odds ratio from Sun (2009) might be due to small sample bias and short NRT treatment course.

The long-term effectiveness of NRT evidence on China is mixed. While Lam (2005) found strong effectiveness of NRT among Hong Kong smokers, Yang (2011) indicated opposite findings that NRT users in China were significantly less likely to quit compared with those who did not use NRT as assistance (OR=0.11 95CI=0.03-0.46). Many factors might contribute to the inconsistent findings, such as research design and study sample characteristics. Details regarding the type of NRT used by smokers, treatment course of NRT, and average daily cigarette consumption are not provided by Yang (2011), while in the study by Lam (2005), it is specified that heavy smokers were given an 8-week course of NRT treatment, which is in compliance with the NRT use guidelines recommended by Western countries (West et al., 2000). The research design of the study by Lam (2005) perhaps contributed to the positive findings showing the effectiveness of NRT. In Yang's (2011) study, it was reported that only 5.8% of smokers in China used NRT and/or Zyban. How NRT was used among Chinese smokers, such as the type of NRT product, dose, and treatment course, remain unknown. The negative effectiveness of NRT found in Yang (2011) suggests a greater need for additional NRT studies.

Although Lam (2005) found NRT significantly increased smoking cessation among Chinese smokers, it is worth mentioning the research location: one was conducted in Hong Kong (Lam et al., 2005), while the other in the Mainland China (Yang et al, 2011). Hong Kong is the most westernized city compared to Mainland China in terms of the social, economic, and cultural context. The smoking pattern in Hong Kong is greatly different from the Mainland China with respect to smoking prevalence, cessation rate, and quitting method use. According to Lopez’s model, the smoking epidemic in Hong Kong is in the advanced stage of smoking epidemic (Lopez et al., 1994), while mainland China is still at the early stage.

Overall, the research evidence on effectiveness of physician counselling and NRT in China healthcare system is dearth.

Chapter 2 Research Objectives

Although studies that estimate the smoking-attributable disease burden in China exist, to the author's best knowledge, there is currently no research on the potentially avoided burden when a smoking cessation intervention is implemented. Population-level smoking cessation interventions have been widely available in Western countries and have demonstrated great impact on increasing smoking cessation in order to prevent smoking-attributable disease burden. Due to the large smoking population and low rate of smoking cessation in China, the smoking-attributable disease burden is expected to soon increase rapidly in China. Given that China has ratified the Framework Convention on Tobacco Control (FCTC), a public health treaty that obligates participating countries to implement a series of tobacco control policies, the implementation of popular smoking cessation interventions in China are anticipated. The extent that future smoking-attributable disease burden may be avoided through physician counselling and NRT in the healthcare system in China needs to be determined to provide insight for public health planning purposes.

The main objective of this study was to investigate the impact of the implementation of physician counselling and NRT in the Chinese healthcare system on smoking-attributable disease burden. This study included two main components. Study 1 used International Tobacco Control (ITC) China project data to estimate the most recent smoking and quitting trends in China, including annual smoking cessation rates among different cigarette consumption groups (light, medium, heavy smokers), and current smoking cessation medication use in China. Study 2 used the available effectiveness evidence data on physician counselling and NRT from Western counties, integrated with China's current smoking and economic data obtained in ITC China project, to predict the potential effectiveness and cost-effectiveness of physician counselling and NRT in healthcare system in urban China.

The research questions for Study 1 and Study 2 were:

Study 1: Smoking and Quitting in China – Findings from ITC China Project

1. How does quitting smoking vary by intention to quit?
2. How do smokers who visit a doctor differ from those not visiting a doctor?
3. What are the quit rates among smokers with and without intention to quit by visiting doctor, cigarette consumption and gender in China?

Study 2: Impact of Physician Counselling and NRT on Disease Burden of Smoking-Attributable Lung Cancer in the Healthcare System of Urban China

1. What is the potential effectiveness of physician counselling on smoking-attributable lung cancer burden among smokers visiting the healthcare system in China?

- Effectiveness of brief physician counselling on all smoking patients (Scenario 1);
- Effectiveness of motivational interview on the smokers not intending to quit (Scenario 2);
- Effectiveness of intensive physician counselling on the smokers intending to quit (Scenario 3);
- Effectiveness of NRT patch on those who smoke more than 10 cigarettes per day with adjunct to intensive physician counselling (Scenario 4).

2. What is the potential cost-effectiveness of physician counselling on smoking-attributable lung cancer burden among smokers visiting healthcare system in China?

- Cost-effectiveness of brief physician counselling on all smokers (Scenario 1);
- Cost-effectiveness of motivational interview on the smokers not intending to quit (Scenario 2);
- Cost-effectiveness of intensive physician counselling on the smokers intending to quit (Scenario 3);
- Cost-effectiveness of NRT patch on those who smoke more than 10 cigarettes per day adjunct to intensive physician counselling (Scenario 4).

Chapter 3 Methods

3.1 Study 1: Smoking and Quitting in China: Findings from the ITC China Project

3.1.1 Sample

Pre-intervention data calculations used data from the ITC project. The ITC China survey is a prospective cohort face to face study conducted in six selected cities in China. The six cities in the ITC China Survey were selected based on geographical representativeness and levels of economic development. In each city, the ITC China Survey employed a multistage cluster sampling design. First, a total of 10 Jie Dao (street district) were randomly selected in each city using the method of Probability of Selection Proportional (PSP) to the population size of the Jie Dao. Second, within each selected Jie Dao, two Ju Wei Hui (residential block) were then again selected according to the population size of the Ju Wei Hui by method of PSP. Third, within each selected Ju Wei Hui, addresses of the dwelling units (households) were listed first and then a sample of 300 households was drawn from the list by simple random sampling without replacement. Information on age, gender and smoking status for all adults living in these 300 households was collected. The enumerated 300 households were ordered randomly, and adult smokers were then approached following the randomized order until 40 adult smokers were surveyed. More detailed study description of the methods of the ITC China Survey can be found elsewhere (Wu, Thompson, Fong, Jiang, Yang, & Feng, 2010).

The ITC China Survey was conducted through face-to-face interviews. All interviewers followed a standard protocol in their interview. Up to four visit attempts to a dwelling unit (household) were made in order to interview the target person(s) within that household. The survey interviewers were trained by the China Centres for Disease Control staff in each city.

Several quality control procedures were used; this included MP3 audio recordings of the smokers' survey by interviewers that were checked by quality controllers in each city. All materials and procedures used in the ITC China Survey were reviewed and cleared for ethics by the Research Ethics Board at the University of Waterloo and by the Institutional Review Boards at the China National Centers for Disease Control and Prevention.

The ITC China Survey is a prospective cohort survey of 800 adult smokers in each of six cities in China: Beijing, Shanghai, Guangzhou, Shenyang, Changsha and Yinchuan. A seventh city

(Zhengzhou) was originally included in Wave 1 and Wave 2 of the ITC China Survey; however, the data from this city were later discarded after data quality testing, and thus Zhengzhou was excluded for the later waves of the ITC China Survey. In order to replenish the sample to its original size, another city (Kunming) was selected as a substitute for Zhengzhou in the ITC China Survey since Wave 3.

The Wave 2 of the ITC China survey included 4,843 smokers (excluding data from Zhengzhou), and Wave 3 included 5,583 (including data from Kunming) (page 7, ITC China Wave Three Technical Report, 2011). A total of 3,923 respondents from Wave 2 were successfully re-contacted from Wave 2 to Wave 3 (81% retention), among which 3,549 were smokers and 374 were abstinent at follow-up. Among 3549 re-contacted smokers, there were a total of 244 who self-reported they had quit smoking at Wave 3, after excluding missing data.

The three waves data of ITC China project were collected during the months of April to August 2006, October 2007 to January 2008, and May to October 2009, respectively.

3.1.2 Measures

Demographics: Age was grouped into the following categories: “18-24; 25-39; 40-54; 55+”. Education level was grouped into “low” (no education & elementary school); “middle” (junior high school & high school); and “high” (college and higher) levels. Monthly household income was grouped as “low” (3000 Yuan and lower), “middle” (3001-5000 Yuan), and “high” (5001 Yuan or higher).

Smoking and quitting status: The respondents included in this study were smokers (smoked 100 cigarettes in their lifetime) at Wave 2 and were re-contacted at Wave 3. Quitting status at Wave 3 was measured by asking, “Do you currently smoke or have you quit?” The respondents who self-reported that they had quit were categorized as quitters. Length of smoking abstinence among quitters was measured. The daily cigarette consumption (cigarette per day or CPD) was measured by the question, “On average, how many cigarettes do you smoke each day, including both factory-made and hand-rolled cigarettes?” Smokers who reported smoking less than or equal to 10 CPD were classified as “light smoker” while the smokers who smoked 11-20 CPD and more than 20 CPD were classified as “medium” and “heavy” smokers, respectively. Smokers’ intention to quit was measured by the question, “Are you planning to quit?” Respondents who reported planning to quit within 6 months were classified as “Intending to quit” while those who did not plan to quit within 6 months were classified as “Not intending to quit.”

Visiting doctor: Smokers’ visit to a doctor at Wave 2 was measured by the question, “Since we last talked to you, have you visited a doctor or other health professional?”

3.2 Study 2: Impact of Physician Counselling and NRT on Disease Burden of Lung Cancer

The estimation on the effectiveness and cost-effectiveness of physician counselling and NRT among Chinese smokers includes two major components: effectiveness and costs.

3.2.1 Calculation of Effectiveness

3.2.1.1 The Comparative Risk Assessment Model

The effectiveness of smoking cessation interventions in this study, including brief physician counselling, intensive physician counselling, and NRT, was estimated using the Comparative Risk Assessment (CRA) Model (Ezzati et al., 2003).

CRA is a tool developed by WHO in 1990 to systematically evaluate the mortality and morbidity attributable to single or group of risk factors, also known as the Population Attributable Fraction (PAF). Conceptually, the PAF is the fraction of the proportion of the incidence of a given health outcome in a given population that is identified as due to the given exposure(s). In general, CRA not only provides the ability to compare disease burden caused between different risk factors, but it can also calculate the future disease burden due to the change of given exposure(s). PAFs of a health outcome were calculated from estimates of the proportion of a population exposed to a risk factor (at various levels, where possible), combined with relative risks of disease or death due to that health outcome resulting from that exposure. Further detailed information on CRA are described elsewhere (Hoorn, Ezzati, Rodgers, Lopez, & Murray, 2004).

In general, the attributable mortality due to a certain risk factor is first estimated from the PAF, described in Equation 1 below (Eide et al., 2001; Ezzati et al., 2004):

$$PAF= (P(RR-1))/(P(RR-1)+1) \quad \text{(Equation 1)}$$

The exposed population to a risk factor may be divided into multiple categories based on the level of intensity of exposure, for which each has its own relative risk. With multiple (m) exposure categories, the PAF is calculated by the following generalized form (Equation 2) (Eide et al., 2001; Ezzati et al., 2004):

$$PAF = \frac{\sum_{i=1}^{m} P_i\,(RR_i - 1)}{\sum_{i=1}^{m} P_i\,(RR_i - 1) + 1} \text{ (Equation 2)}$$

In Equation 2, the reference exposure level chosen was zero. In order to compare the disease burden due to observed or potentially expected change on exposure distribution, rather than using a zero reference level, the PAF is further generalized as the Potential Impact Fraction (PIF), described in Equation 3 (Eide et al., 2001; Ezzati et al., 2004):

$$PIF = \frac{\sum_{i=1}^{m} p_i RR_i - \sum_{i=1}^{m} p'_i RR_i}{\sum_{i=1}^{m} p_i RR_i} \text{ (Equation 3)}$$

With the estimate of PIF, mortality from disease *j* due to the certain risk factor *i*, attributable burden (AB) was calculated using Equation 4 (Eide et al., 2001; Ezzati et al., 2004):

$$AB_{Ji} = Potential\ Impact\ Fraction \times total\ disease\ burden_{ji} \text{ (Equation 4)}$$

3.2.1.2 Impact of Physician Counselling and NRT on Disease Burden of Lung Cancer

Based on the CRA model, the impact of physician counselling and NRT were estimated by the discrepancy between the disease burden of lung cancer observed currently with the hypothetically assumed physician counselling and NRT implemented in China's healthcare system. To estimate their impact, the relative risk for lung cancer and risk exposure level before and after the implementation of physician counselling and NRT must be determined. However, according to CRA model, an assumption is that the major determinant of the variation in the attributable disease burden due to a certain risk factor is not a function of differences in relative risk; rather, the difference in exposure level of the risk factor is wholly responsible (Murray, & Lopez, 1999). Therefore, in this study, the variation of disease burden of lung cancer was assumed to be the only cause of discrepancy in smoking prevalence from the implementation of physician counselling and NRT.

The current lung cancer mortality in China serves as pre-intervention data. There were two reasons for using current general lung cancer mortality for the pre-implementation calculation. First, there is no well-established physician counselling and NRT routinely available in healthcare system in China. Second, although there is limited physician counselling provided in China, findings suggest physician counselling does not impact smoking cessation (Yang et al., 2010). The evidence on the effectiveness on NRT in China was mixed (Sun et al., 2009; Yang et al., 2010; Yu et al., 2006).

A risk factor in this study examined active smoking only; passive smoking was excluded. The selected smoking-attributable disease was lung cancer. The smoking-attributable disease burden was calculated for lung cancer among smokers.

Current exposure levels to smoking were measured by current smoking prevalence obtained from the best existing evidence of China. The smoking prevalence after implementation of physician counselling and NRT was estimated by deducting increased smoking cessation rate due to the implementation of physician counselling and NRT from current smoking prevalence in China. Since there is limited effectiveness research on physician counselling and NRT in China, the best evidence on the effectiveness of physician counselling and NRT from Western countries was applied to calculate the increased quit rate to estimate the after-intervention smoking prevalence. In the current study, a total of four scenarios of physician counselling and NRT intervention designed for healthcare system in China were assessed: (1) brief physician counselling provided to all smokers visiting healthcare system in China; (2) motivational interview provided to smokers who don't intend to quit smoking; (3) intensive smokers provided to all smokers who intend to quit; and (4) NRT patch adjunct to physician counselling provided to medium/heavy smokers (CPD>10) who intend to quit.

Robust evidence from Western countries suggests that physician counselling is effective for general smokers, while NRT is most effective for the smokers who smoke more than 10 to 15 CPD (Fiore, 2008). The four scenarios of physician counselling and NRT designed in this study were not only based on the best evidence demonstrated by existing literature from Western countries and available data in China, but also take China's realistic issues into account in order to present the impact of physician counselling and NRT by different intensity levels.

3.2.1.3 Data Selection

As mentioned earlier in this paper, the calculation of effectiveness of physician counselling and NRT by the CRA model mainly involve two categories of key indicators: smoking prevalence and corresponding relative risk. For the ideal scenario calculation, the smoking prevalence and the relative risks used should be well matched, but in practice, valid and reliable data on well-matched relative risks and corresponding smoking prevalence are usually lacking.

For the present study, the calculation of pre- and after- interventions lung cancer disease burden involved: (1) pre-intervention, or current smoking prevalence; (2) after-intervention smoking prevalence; and (3) relative risk of lung cancer, assumed unchanged between pre- and after intervention.

In order to match relative risks of lung cancer and smoking prevalence as much as possible in the calculation of Study 2, Study 1 conducted necessary statistical tests to examine the significant difference between quit rates among different smoking groups, which were subsequently used to calculate the after- intervention smoking prevalence when alternative relative risks were applied.

Basically, pre-intervention or current smoking prevalence and relative risk of lung cancer caused by smoking were directly obtained from best available evidence in China. The after-smoking prevalence in China was calculated by the effectiveness of physician counselling and NRT obtained from Western countries and smoking cessation rates in Study 1 from the ITC China project. For smoking prevalence data selection, the main principle is the most recent national study conducted in China; for the relative risk of lung cancer and effectiveness of physician counselling and NRT, the primary selection criterion is large-scale meta-analysis. The relative risks of smoking-attributable lung cancer and smoking prevalence in each category were matched as much as possible. Table 5.1 shows the detailed data selection sources.

Table 3.1 Key Value Selection for Calculation:

Indicator	Role in Calculation	Selected Source	Reason for Selection	Key Value Selected
Pre-intervention (current) smoking prevalence	Directly apply to CRA model for pre-intervention disease burden	Prevalence of smoking in China in 2010 (Li, 2011) Project: Global Adult Tobacco Survey (GATS) conducted in 2010 Prevalence of smoking in China in 2010 (Li, 2011) N Engl J Med. 2011 Jun 23;364(25):2469-70.	Most recent; representative data in China	Smoking prevalence in Urban area: Overall: 26.1% Male: 49.2% Female: 2.6%
Current Smoking Cessation Rates in China	Together with effectiveness of physician counselling to calculate the after-intervention quit rate	First hand data calculation using ITC China Data	Most recent, representative data in China	Obtained in Study 1
Effectiveness of Physician Counselling	Together with current smoking cessation rate to calculate after-intervention quit rate	Lai DTC, Cahill K, Qin Y, Tang JL. Motivational interviewing for smoking cessation. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD006936. DOI: 10.1002/14651858.CD006936.pub2		Motivational interviewing is effective (RR = 1.27, CI = 1.14–1.42)
		Stead LF, Bergson G, Lancaster T. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD000165. DOI: 10.1002/14651858.CD000165.pub3.	Most recent, updated meta-analysis; clear intervention description	Brief counselling vs.no counselling 1.66 (1.42, 1.94) Intensity counseling Vs. no counselling 1.84 (1.60, 2.13)
Effectiveness of NRT	Together with current smoking cessation rate to calculate after-intervention quit rate	Fiore MC (2008). A clinical practice guideline for treating tobacco use and dependence: 2008 update. A US Public Health Service report		NRT patch: 1.9 (1.7, 2.3) For both 6-14 weeks use or longer than 14 weeks
Effectiveness of NRT plus intensive counselling	Together with current smoking cessation rate to calculate after-intervention quit rate	Fiore MC (2008). A clinical practice guideline for treating tobacco use and dependence: 2008 update. A US Public Health Service report		Medication plus counseling vs. counselling alone 1.7 (1.3–2.1)
Relative Risk of Lung Cancer Caused by Smoking	Apply to CRA model, unchanged between pre and after interventions	Emerging tobacco hazards in China: 1. Retrospective proportional mortality Study of one million deaths. (Liu, 1998)	Retrospective cohort study of one million death	Male: 2.98 (SE:0.05) Female: 3.24 (SE: 0.08) CPD <10: 2.08(SE: 0.05) CPD 10-19: 3.59 (SE:0.06) CPD >=20: 6.92 (SE: 0.14)

3.2.2 Calculation of Cost

Evidence from Western countries indicates that the major costs for physician counselling and NRT are physician salary and NRT retail price (Cornuz et al., 2003). Therefore, in this study, the costs of physician counselling and NRT were calculated based on Chinese physician salary and the NRT local price in China.

According to the most recent systematic review from US (Fiore et al., 2008), brief physician counselling is defined as quitting advice lasting 3 to 10 minutes in duration provided by a physician when a smoker visits a doctor. Intensive physician counselling is defined as a 20-minute long professional smoking cessation counselling session, with two follow-up visits that would each take 20 minutes (Fiore et al., 2008). It is particularly emphasized that intensive physician counselling on smoking cessation should be provided by a trained physician or health professional (Fiore et al., 2008). A smoking cessation handbook is also provided to smokers who receive intensive physician counselling. NRT will be prescribed to the smokers who receive intensive physician counselling.

All costs were calculated in US dollars (USD) and relate to prices in 2008. All costs used in this study are assumed to occur in the same year and are not discounted. This study thus employs a prevalence rather than an incidence methodology.

3.2.3 Economic Analysis on Implementation of Physician Counselling and NRT in Healthcare System in China

The effectiveness of physician counselling and NRT in the healthcare system of China are presented by additional quitters generated and the avoidable smoking-attributable lung cancer among Chinese smokers.

In order to conduct economic analysis, further calculation needed to be performed in order to convert the effectiveness results, the additional quitters and the avoidable lung cancer deaths estimated, in monetary terms.

The costs of implementing physician counselling and NRT patch are mainly calculated by the cost of physician time and the retail price for an NRT patch in China. According to the evidence base, the most recent practical guidelines for treating tobacco, the time spent on motivational interview, brief counselling and intensive counselling is defined as 15-45 minutes, 3-10 minutes and 20-80 minutes respectively The indirect costs, such as patient commuting time or time spent during office visits were not included. Total costs of implementation of each scenario were calculated by multiplying cost for each smoker receiving service with the total target smoking population.

Cost-effectiveness results were calculated by cost of each additional quitter generated and the total cost savings (including direct medical cost and indirect productivity cost) on smoking-attributable lung cancer mortality by implementing physician counselling.

The additional quitters generated by each scenario were estimated by multiplying the increased quit rates obtained from Study 1 with the target smoking population. The cost per quitter was calculated by dividing the total cost by total additional quitters generated.

Yang (2011) provided an updated estimate of economic cost attributable to smoking in China in 2008. Based on the research findings, the average economic cost per lung cancer patient could be calculated. By multiplying the individual expense to avoidable disease burden on lung cancer, the total economic savings on smoking-attributable mortality by implementing physician counselling and NRT were estimated.

Economic costs were calculated from a societal perspective based on real resources required. For the unit costs of counselling, the average salary of a healthcare employee per minute was used. For the NRT patch costs in Scenario 4, the unit cost per patch is the average price of major brands in China's retail market, and the total NRT patch cost for each selected smoker was calculated based on the recommended usage reported in clinical guidelines (Fiore et al., 2008). All costs were calculated in USD and related to prices in 2008, the year the data were related. Because no analysis of long-term benefits was intended, costs and outcomes were not discounted.

A sensitivity analysis was conducted mainly by varying and adding additional costs.

3.2.4 Analysis

Statistical analyses in Study 1 were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC). Analyses were weighted by sex and age in order to be representative within each city and to account for the sampling design of the ITC survey. Survey frequency tests were used to estimate the percentages presented in this paper. Contrast tests were used to estimate the distribution differences by gender and cigarette consumption. Survey logistic regressions were conducted to test the difference in quitting, intention to quit and visiting doctor, and to calculate the mean quit rate in defined groups.

Calculations in Study 2 were performed using Microsoft Excel 2010, supplemented by manual calculation when necessary.

Chapter 4 Results

4.1 Study 1

4.1.1 Sample Characteristics

A total of 3,714 of smokers from Wave 2 were re-contacted in Wave 3, of which 518 smokers (approximately 14%) smoked more than 20 CPD (heavy smokers); 1,801 (approximately 48%) smoked 11- 20 CPD (medium smokers); and 1,395 smoked less than 10 CPD (light smokers) (approximately 38%) (Table 4.1 & Table 4.2).

The distribution of heavy, medium, and light smokers were significantly different by age group ($p<0.005$ for all pairwise contrasts). There were no heavy smokers in the age group of 18-24 and more than half (53.6%) of smokers aged 40-54 were heavy smokers. Older age groups (40-55; 55+) were significantly more likely to be heavy smokers relative to younger age groups. Female smokers were more likely to be light smokers (medium vs. light: $p <0.001$; heavy vs. light: $p=0.0011$), but there was no gender difference between medium versus heavy smokers ($p=0.59$).

Table 4.1: Sample Characteristics from ITC China Wave 2:

		Heavy smokers (CPD>=20) N (%)	**Medium smokers (CPD 11-20) N (%)**	**Light smokers (CPD <=10) N (%)**	**Total N (%)**
Sex	Male	500 (97.86%)	1,728 (97.55%)	1,287(94.10%)	3,515 (96.27%)
	Female	18 (2.14%)	73 (2.45%)	108 (5.90%)	199 (3.73%)
Age	18-24	0 (0)	12 (0.56%)	23 (2.21%)	35 (1.11%)
	25-39	61 (9.90%)	261(13.85%)	236 (16.72 %)	558 (14.40%)
	40-54	285 (53.57%)	963 (52.37%)	592 (41.57%)	1,840 48.39%)
	55+	172 (36.53%)	565 (33.23%)	544 (39.49%)	1,281 36.09%)
Income	Low	88 (14.33%)	302 (16.06%)	199 (14.02%)	589 (15.03%)
	Medium	254 (54.25%)	795 (47.51%)	628 (49.47%)	1,677 49.21%)
	high	141 (31.42%)	584(36.43%)	467 (36.51%)	1,192 35.75%)
Education	Low	73 (12.281%)	193 (10.20%)	172 (12.06%)	438 (11.20%)
	Medium	367(72.90%)	1248 (71.09%)	885 (63.80%)	2,500 68.54%)
	High	74 (14.81%)	346 (18.71%)	333 (24.14%)	753 (20.26%)

Table 4.2 Smoking and Quitting by Gender:

		Male		Female		Total	
		N	**%**	**N**	**%**	**N**	**%**
Daily Cigarette Consumption	**Light Smoker (CPD=<10)**	1287	37.54%	108	60.68%	1395	38.40%
	Medium Smoker (11<CPD<20)	1782	48.25%	73	31.31%	1801	47.62%
	Heavy Smoker (CPD>=20)	500	14.21%	18	8.01%	518	13.98%
	Total	3569	100%	199	100%	3714	100%
Intention to quit	**Intending to quit in 6 months**	489	13.85%	39	18.51%	528	14.06%
	Not intending to quit in 6 months	2800	86.15%	145	81.49%	2945	85.94%
	Total	3289	100%	184	100%	3473	100%
Abstinent follow-up	**Yes**	228	6.70%	16	5.92%	244	6.67%
	No	3297	93.30%	185	94.08%	3482	93.33%
	Total	3525	100%	201	100%	3726	100%

4.1.2 Quitting by Doctor Visiting and Cigarette Consumption

Among medium and light smokers, the quit rates were 4.7% and 10.2%, respectively. In contrast, among heavy smokers, the quit rate was 3.68% (only 22 individuals). The results from contrast tests show that light smokers in China were more likely to quit smoking (medium vs. light: $p < 0.001$; heavy vs. light: $p=0.0012$) than heavy and medium smokers, while there was no significant difference observed for quitting between medium and heavy smokers ($p=0.6158$).

The percentage of intention to quit at Wave 2 was lowest among heavy smokers (7.19%) and increased to 11.02% among medium smokers, then further increased to 20.44% among light smokers in China. Contrast tests suggested light smokers were more likely to intend to quit smoking (medium vs. light: $p < 0.001$; heavy vs. light: $p=0.001$), but there was no significant difference on quit intention between medium and heavy smokers ($p=0.0541$).

A logistic regression model was conducted to examine quitting differences between the smokers intending to quit and the smokers not intending to quit, adjusting for sex, age and daily cigarette consumption. Smokers intending to quit were 2.06 times more likely to self-report being abstinent at follow up (95%CI=1.49-2.85; $P<.0001$).

Another logistic regression model was conducted to test for differences in intention to quit among smokers visiting a doctor and smokers not visiting a doctor after adjusting for age, sex, and daily cigarette consumption. The results show that smokers who visited doctors were significantly more likely to intend to quit smoking within six months (17.95%), compared with smokers who did not visit a doctor (11.32%;OR=1.71, CI95=1.32-2.23).

An additional logistic regression model was conducted to test the differences in quitting among smokers visiting doctor and not visiting doctor, adjusting for age and daily cigarette consumption. Significantly higher quit rates among smokers visiting doctor relative to their counterparts of not visiting doctors were found (Table 4.3). Overall, smokers in China who visited a doctor or health professional were 1.53 times more likely to quit smoking (95%CI=1.10-2.13) than those who did not visit a doctor.

Among smokers visiting doctors, additional analyses were conducted to test the gender differences on frequency (distributions) of not intending to quit, intending to quit and cigarette consumption by intention to quit. The results show no significant difference in the frequency (distributions) between male and female smokers who visited doctors in intending to quit, not intending to quit, and cigarette consumption by intention to quit ($p>0.05$ in all cases). Similarly, there was no significant difference between male and female smokers who visited doctors in terms of the quit rate ($p>0.05$ in all cases). Given that the sample had less than 200 female smokers, it was under-powered to test for gender differences in subgroups.

In summary, the results from Study 1 identified important characteristics of Chinese smokers. Light smokers (CPD≤10) in China were more likely to intend to quit and being quit at follow up compared with their counterparts of medium (10<CPD≤20) and heavy (CPD>20) smokers. Smokers who intended to quit were significantly more likely to quit smoking, in contrast to the smokers without intention to quit in China. Smokers who visited a doctor were significantly more likely to intend to quit and to have successfully quit at follow up, compared with those not visiting doctors. Among smokers visiting doctor, there was no gender difference in intention to quit, no intention to quit and cigarette consumption by intention to quit.

These findings highlight that light smokers and smokers visiting doctors had different characteristics relative to their counterparts of medium/heavy smokers and smokers who do not visit a doctor.

Since the major purpose of the present study was to investigate the effectiveness and cost-effectiveness of physician counselling and NRT among smokers visiting a doctor, additional logistic models were conducted to further examine the mean quit rates among the smokers who visited doctors with the intention to quit as well as those without the intention to quit among males and females, respectively, adjusting for age and daily cigarette consumption (Table 4.4).

Table 4.3: Quit Rates among Smokers Visiting Doctor and Not Visiting Doctor

		Mean Quit rate	Confidence Interval	
Male	Visiting Doctor	7.68%	6.00%	9.79%
	Not visiting Doctor	5.36%	4.31%	6.66%
	Visiting Doctor vs. Not visiting Doctor	OR: 1.47	1.03	2.09
Female	Visiting Doctor	11.43%	5.48%	22.30%
	Not visiting Doctor	3.26%	1.15%	8.90%
	Visiting Doctor vs. Not visiting Doctor	OR: 3.83	0.89	16.53
All	Visiting Doctor	7.81%	6.20%	9.79%
	Not visiting Doctor	5.23%	4.21%	6.50%
	Visiting Doctor vs. Not visiting Doctor	OR: 1.53	1.10	2.13

Table 4.4: Quit Rates among Smokers Visiting Doctors

		Daily Cigarette Consumption	Mean Quit Rate	Confidence Interval	
Smokers Intending to Quit	**All**	Overall	12.46%	9.56%	16.09%
		Light	19.48%	14.06%	26.34%
		Medium	9.61%	6.91%	13.21%
		Heavy	8.90%	5.39%	14.35%
	Male	Overall	12.61%	9.65%	16.32%
		Light	19.70%	14.22%	26.63%
		Medium	9.73%	6.99%	13.39%
		Heavy	9.02%	5.43%	14.60%
	Female	Overall	9.48%	5.53%	15.79%
		Light	14.84%	8.22%	25.29%
		Medium	7.11%	3.90%	12.60%
		Heavy	6.58%	3.49%	12.04%
Smokers Not Intending to Quit	**All**	Overall	6.71%	5.15%	8.70%
		Light	10.98%	7.73%	15.35%
		Medium	5.14%	3.80%	6.92%
		Heavy	4.74%	2.76%	8.05%
	Male	Overall	6.79%	5.19%	8.86%
		Light	11.12%	7.82%	15.58%
		Medium	5.21%	3.84%	7.05%
		Heavy	4.81%	2.78%	8.21%
	Female	Overall	5.02%	2.98%	8.36%
		Light	8.16%	4.50%	14.35%
		Medium	3.75%	2.13%	6.52%
		Heavy	3.47%	1.83%	6.49%

4.2 Study 2

4.2.1 Effectiveness of Physician Counselling and NRT Patch in Healthcare System in China

4.2.1.1 Main Results

The main purpose of Study 2 was to use the smoking and quitting results from Study 1 and integrate them with population data to broaden the effects to the population level.

Although six participating cities in the ITC China project were selected based on geographic representativeness and levels of economic development, they were not theoretically urban representative. Additional analysis was conducted to test if the ITC China sample could be statistically inferred to urban areas of China. Briefly speaking, for each sample city, the three-way frequency calculation of the quit rate quit rate by age group crossed with daily cigarette consumption was tested. The results (not shown) indicated that there was a significant difference but similar estimate between the quitting rates across cities overall. The fact that the six sampling cities in ITC China Survey were selected based on geographical representativeness and levels of economic development, it is therefore reasonable to assume the ITC sample represented urban China.

Due to the overall small sample size of female smokers (N=184) in ITC China project, when decomposed to female smokers intending to quit (N=39) and female smokers not intending to quit (N=145) for calculating mean quit rates among the two groups separately, the results either fail to provide the mean quit rate in certain category (female heavy smokers not intending to quit) due to the unavailable sub-sample, or provided impractically large confidence intervals (i.e. quit rate for female heavy smokers intending to quit: 12.46% with confidence interval of 0.42% to 82.94%). Further analyses were conducted to test the quit rate difference between male and female among the smokers who visited doctors by intention to quit, no intention to quit rate, and cigarette consumption within intention to quit. The results indicated there were no significant differences on quit rates in all cases ($p>0.05$ in all cases). Hence, for the following related calculations for females, instead of using the female-specific quit rates estimated in Study 1, the quit rate for male smokers in corresponding categories were applied for the female group. For the calculations for males, the male-specific quit rates from Study 1 were applied.

The results of Study 1 also indicated significant differences between light smokers and medium/heavy smokers in China. Briefly speaking, light smokers were more significantly intending to quit than medium and heavy smokers (medium vs. light: $p < 0.001$; heavy vs. light: $p=0.001$), and there was no statistical difference between medium and heavy smokers ($p=0.0541$). Combined with the recommendation of US Clinical Practice Guidelines for Treating Tobacco Use and Dependence (Fiore, 2008), in which intensive physician and NRT are suggested only for smokers intending to quit and smokers whose daily cigarette consumption more than 10, four scenarios of smoking cessation interventions were designed for China healthcare system described below:

Scenario 1: Brief counselling to ALL smokers;

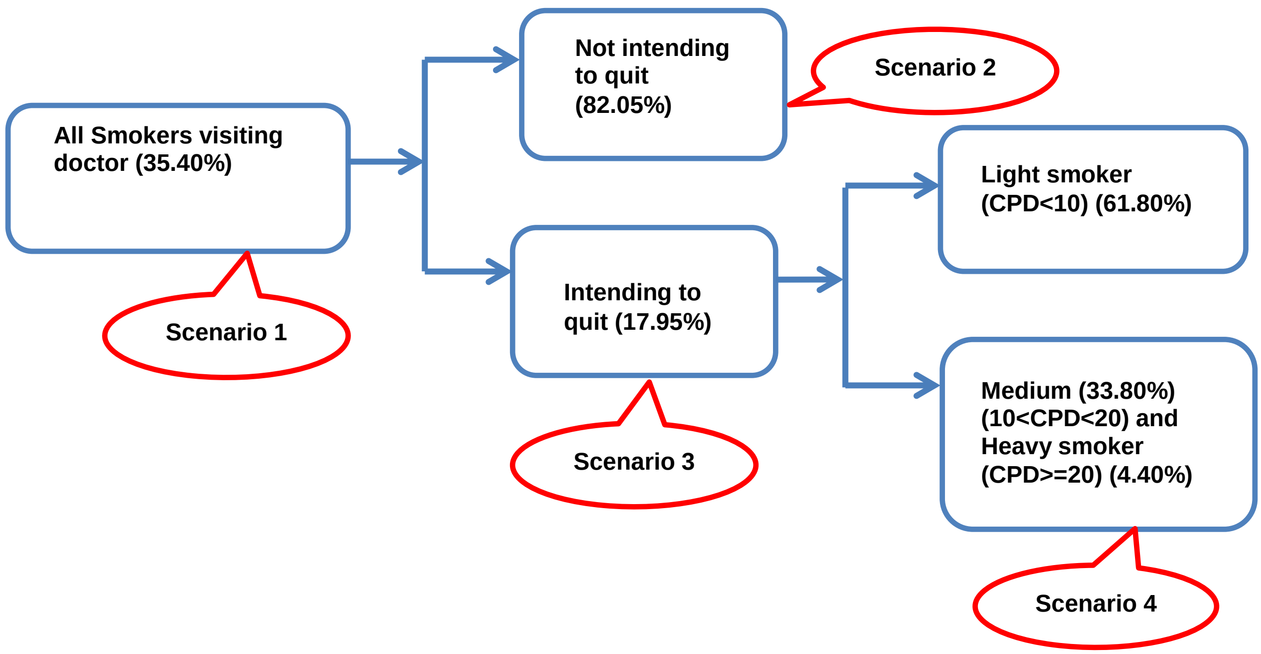
Scenario 2: Motivational interview to ALL smokers NOT intending to quit;

Scenario 3: Intensive counselling to ALL smokers intending to quit;

Scenario 4: Intensive counselling to only the smokers intending to quit AND being either medium/heavy smokers (CPD>10).

Given the results from Study 1 of ITC China project was conducted in six urban cities in China, the four scenarios were only calculated for urban China.

Figure 4.1: Smokers Visiting Healthcare System in Urban China in 2008



To calculate the smoking-attributable fraction of lung cancer, the following epidemiological equation (Equation 1) (Lilienfeld, & Lilienfeld, 1994) was applied:

$$PAF= (P(RR-1))/(P(RR-1)+1) \quad \text{(Equation 1)}$$

In Equation 1, RR and P denote the relative risks for the lung cancer and smoking prevalence. The PAF was calculated for total death of lung cancer caused by smoking. The detailed key values applied in the calculation as well the data source are listed in Table 3.1. PAF was calculated at before and after implementation of physician counselling and NRT in China. For each scenario, the calculation was divided into three main sections:

- Pre-intervention smoking-attributable lung cancer burden in urban China;
- After-intervention smoking-attributable lung cancer burden in urban China;
- Difference of before and after implementation of each scenario.

According to Equation 1, the PAF of lung cancer caused by smoking was calculated by risk exposure, or smoking prevalence in this case, and relative risks by different categories. During the calculation of the designed scenarios, relative risks of smoking-attributable lung cancer were consistent by categories across the calculation. The results of smokers' distribution by differently defined categories calculated in Study 1 were used in the pre-intervention smoking prevalence calculation. The quit rates from Study 1 together with the effectiveness of physician counselling and NRT withdrawn from the Western studies were used to calculate the after-intervention smoking prevalence. For each scenario, the discrepancy of the smoking-attributable fractions calculated from smoking prevalence of pre- and after- intervention was enlarged with population lung cancer data to estimate the avoided lung cancer burden among smokers. Ideally, for the calculation of each scenario designed in Study 2, all the values involved need to be well matched for the calculated category. Due to the small female sample size, it was a challenge for quit rates calculated for female smokers to reflect the overall quitting situation among Chinese female smokers. Therefore, the quit rates for male smokers in corresponding smoking category were applied to female calculations.

Theoretically, for each PAF calculation, the smoking prevalence for the pre- and after designed scenario and the relative risks of lung cancer caused by smoking should be well-matched. Although the calculations of Study 2 were based on the best evidence from existing research findings from Western countries, China, and Study 1, there were still some gaps between the data needed and the data available. Therefore, some reasonable assumptions during the calculation of Study 2 were necessary. After adjusting the overall available evidence from Western and China, the following assumptions were made for Study 2 (Table 4.5):

Table 4.5: Assumptions for Study 2

Scenario		**Assumptions**
1	Brief counselling to ALL smokers	Quit rate of male smokers visiting doctor equals to quit equals to female smokers visiting doctor
2	Motivational interview to ALL smokers NOT intending to quit	Quit rate of male smokers visiting doctor AND not intending to quit equals to their female counterparts.
3	Intensive counselling to ALL smokers intending to quit	Quit rate of male smokers visiting doctor AND intending to quit equals to their female counterparts.
4	Intensive counselling plus NRT patch to medium/heavy smokers (CPD>10)	Quit rate of medium/heavy male smokers (CPD>10) visiting doctor AND intending to quit equals to their female counterparts;
		Mortality relative risk of smoking-attributable lung cancer among male medium smokers (10<CPD≤20) equals to their female counterparts;
		Mortality relative risk of smoking-attributable lung cancer r among male heavy smokers (CPD>20) equals to their female counterparts

In China, the total population over 15 years old in urban areas was approximately 491.59 million (China Health Statistics Year Book, 2009), among which about 26.1% were smokers (Li et al., 2011), resulting in a total of 128.30 million urban population of current smokers aged 15 years older in China (Table 4.6). By multiplying the smoking prevalence of male and female with the corresponding population reported in the China Health Statistics Yearbook 2009, China had a total of 124.56 million male smokers and 6.20 million female smokers in urban areas (calculation shown in

Table 4.7). Among urban male smokers in China, almost two thirds (62.5%) or 77.8 million people were heavy and medium smokers who smoked more than 10 cigarettes each day. The majority of female smokers (60.7%) in urban China were light smokers, defined as 10 or fewer CPD, accounting for 3.76 million smokers (Table 4.8).

Table 4.6: Smoking Prevalence in Urban China in 2010

	Smoking Prevalence
Overall over 15 years old	26.1% [1]
Male over 15 years old	49.2% [1]
Female over 15 years old	2.6%[1]
Children under 15 years old	1.12% for 6-14 years old [2] Not available for children under 6 years old

[1] Li, Q.(2011) [Smoking prevalence refers to smoking prevalence at the survey time, measured by the question of " are you currently smoking?"; Daily smoking is defined as the smokers who reported smoking daily at the survey time]; [2] Cao, R.X. (2008) Epidemiological analysis of tobacco use among children and adolescents in Beijing.[Smoking prevalence is measured by the question of "did you smoking in the last 30 days?", the children who reported smoking at least one cigarette were classified as children smokers].

Table 4.7: Distribution of Smoking Population in Urban China in 2008

Demographic Category	**Percentage**	**Total Population (in millions)**	**Smoking Population (in millions)***
Total population	--	1,328.02[1]	--
Total urban population	45.7%[1]	606.91	--
Population over 15 years old overall	81%[1]	491.59 (606.91×81%[1])	128.30 (491.59×26.1%[2])
Male over 15 years old	51.5%[1]	253.17 (491.59×51.5%[1])	124.56 (253.17×49.2%[2])
Female over 15 years old	48.5%[1]	238.42 (491.59×48.5%[1])	6.20 (238.42×2.6%[2])

[1] China Health Statistics Year Book (2009);
2 Li, Q. (2011)

Table 4.8: Smoking Prevalence by Cigarette Consumption in Urban China in 2008:

Daily Cigarette consumption	**Male**		**Female**		**Total**	
	%	**Population (in millions)**	**%**	**Population (in millions)**	**%**	**Population (in millions)**
Light smoker (<10 CPD)	37.54%[1]	46.76	60.68%[1]	3.76	38.40%	50.52
Medium smoker (10-19 CPD)	48.25%[1]	60.10	31.31%%[1]	1.94	47.62%	62.04
Heavy smoker (≥20 CPD)	14.21%[1]	17.70	8.01%%[1]	0.50	13.98%	18.20
Total	100%	124.56	100%	6.20	100%	130.76

[1] calculated in Study 1

According to the China Health Statistics Book (2009), the mortality of lung cancer in urban China was 63.59 and 32.63 per 100,000 among males and females, respectively. Multiplied with the corresponding population, the smoking-attributable lung cancer deaths in China in 2008 was estimated to be approximately 237.2 thousand, among which 161 thousand were male and 77.8 thousand were female (Table 4.9).

Table 4.9: Total Deaths from Lung Cancer among Adults in Urban China in 2008:

	Total death (in thousands)
Male	(63.59[1]/100,000)*253170000[1]=160,991 (161.0 thousand)
Female	(32.62[1]/100,000)*238420000[1]=77,773 (77.8 thousand)
Total	(48.25[1]/100,000)*491590000[1]=237,192 (237.2thousand)

[1] China Health Statistics Year Book (2009), Ministry of Health of the People's Republic of China, Peking Union Medical College.

Table 4.10 Results of Effectiveness of Physician Counselling and the NRT Patch

Scenario1: Brief Counselling to All Smokers

		Values of Smoking Prevalence used in PAF calculation	Values of Relative Risk of Lung Cancer Used in PAF Calculation	PAF to Lung Cancer	Pre-After Difference	
					%	Life saved
Pre-intervention	**Male**	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Prevalence of male smokers visiting doctor: 49.2%×35.4%=17.417%	Male: 2.98 (SE:0.05) 2	25.643%	--	--
	Female	Female: 2.6% [1] Female smokers visiting doctor: 35.40% Prevalence of female smokers visiting doctor: 2.6%×35.4%=0.920%	Female: 3.24 (SE: 0.08) 2	2.019%	--	--
After-intervention	**Male**	Prevalence of male smokers visiting doctor: 17.417% Pre-Quit rate: 7.68% [4] After-Quit rate (male) 7.68%×1.66[5]=12.75% Quit rate increased=12.75%-7.68%=5.07% After-intervention smoking prevalence=17.417%-5.07%×17.417%=16.534%	Male: 2.98 (SE:0.05) 2	24.663%	25.643%-24.663%= 0.979%	160,991×0.979%=1577
	Female	Prevalence of visiting female smokers intending to quit: 0.920% Pre-Quit rate: 7.68%	Female: 3.24 (SE: 0.08) 2	1.920%	2.019%-1.920%= 0.099%	77,773×0.099%=77

		After-Quit rate (female) 7.68%×1.66^{5}=12.75% Quit rate increased=12.75%-7.68%=5.07% After-intervention smoking prevalence=0.920%-5.07%×0.920%=0.874%				
Total						1,654

1.Li, (2011);
2 Liu,(1998);
3.Yu, (1996);
4.Results from study 1.
5.Stead LF (2008).
6.Lai DTC (2010)
7.Fiore MC (2008).

Scenario 2: Motivational Interview among All Smokers Not Intending to Quit

		Values of Smoking Prevalence used in PAF calculation	Values of Relative Risk of Lung Cancer Used in PAF Calculation	Population Attributable Fraction(PAF) to Lung Cancer	Pre-After Discrepancy	
					%	Lung Cancer Death Avoided
Pre-intervention	**Male**	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Male smokers NOT intending to quit 82.05% Prevalence of visiting male smokers NOT intending to quit: 49.2%×35.4%×82.05%=14.290%	Male: 2.98 (SE:0.05) 2	22.054%	--	--
	Female	Female: 2.6% [1] Female smokers visiting doctor: 35.40% Female smokers NOT intending to quit 82.05% Prevalence of visiting female smokers NOT intending to quit: 2.6%×35.4%×82.05%=0.755%	Female: 3.24 (SE: 0.08) 2	1.663%	--	--
After-intervention	**Male**	Male: 14.290% Pre-Quit rate (male): 6.79% [4] After-Quit rate (male) $6.79\% \times 1.27^6 = 8.62\%$ Quit rate increased=8.62%-6.79%=1.83% After-intervention smoking prevalence=14.290%-1.83%×14.290%=14.028%	Male: 2.98 (SE:0.05) 2	21.738%	22.054%-21.738%= 0.316%	160,991×0.316%=510
	Female	Female: 0.755% Pre-Quit rate: 6.79% [4] After-Quit rate (female) $6.79\% \times 1.27^6 = 8.62\%$ Quit rate increased=8.62%-6.79%=1.83%	Female: 3.24 (SE: 0.08) 2	1.633%	1.663%-1.633%= 0.030%	77,773×0.030%=24

		After-intervention smoking prevalence=0.755%-1.83%×0.755%=0.741%				
Total						534

Scenario 3: Intensive Counselling among All the Smokers Intending to Quit

		Values of Smoking Prevalence used in PAF calculation	Values of Relative Risk of Lung Cancer Used in PAF Calculation	Population Attributable Fraction(PAF) to Lung Cancer	Pre-After Discrepancy	
					%	Life saved
Pre-Intervention	**Male (CPD≤10)**	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Male smokers intending to quit 17.95% Male smokers intending to quit AND being light smoker (CPD≤10) Prevalence of visiting doctor, male, light smokers intending to quit: 49.2%×35.4%×17.95%×61.80%=1.932%	2.08	2.044%	/	/
	Male (11<CPD<19)	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Male smokers intending to quit 17.95% Male smokers intending to quit AND being light smoker (11<CPD<19) Prevalence of visiting doctor, male, medium smokers intending to quit: 49.2%×35.4%×17.95%×33.80%=1.057%	3.59	2.665%	/	/
	Male (CPD>20)	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Male smokers intending to quit 17.95% Male smokers intending to quit AND being light smoker (CPD>20) Prevalence of visiting doctor, male, heavy smokers intending to quit: 49.2%×35.4%×17.95%×4.40%=0.138%	6.92	0.810%	/	/
	Female (CPD≤10)	Female: 2.6% [1] Female smokers visiting doctor: 35.40% Female smokers intending to quit 17.95% Prevalence of visiting doctor, female, light(CPD≤10) smokers intending to quit: 2.6%×35.4%×17.95%×61.80%=0.102%	2.08	0.110%	/	/
	Female	Female: 2.6% [1]	3.59	0.145%	/	/

	(11<CPD<19)	Female smokers visiting doctor: 35.40% Female smokers intending to quit 17.95% Prevalence of visiting doctor, female, medium (11<CPD<19) smokers intending to quit: 2.6%×35.4%×17.95%×33.80%=0.056%				
	Female (CPD>20)	Female: 2.6% [1] Female smokers visiting doctor: 35.40% Female smokers intending to quit 17.95% Prevalence of visiting female smokers intending to quit: 2.6%×35.4%×17.95%×4.40%=0.007%	6.92	0.041%	/	
After-intervention	**Male (CPD≤10)**	Prevalence of visiting doctor, male, light smokers intending to quit: 1.932% Pre-Quit rate: 19.70% After-Quit rate (male) 19.70%×1.84=36.25% Quit rate increased =36.25%-19.70%=16.55% After-intervention smoking prevalence=1.932%-16.55%×1.932%=1.612%	2.08	1.711%	2.044%-1.711%=0.333%	536
	Male (11<CPD<19)	Prevalence of visiting doctor, male, medium smokers intending to quit: 1.057% Pre-Quit rate: 9.73% After-Quit rate (male) 9.73%×1.84=17.90% Quit rate increased =17.90%-9.73%=8.17% After-intervention smoking prevalence=1.057%-8.17%×1.057%=0.971%	3.59	2.453%	2.665%-2.453%=0.212%	340
	Male (CPD>20)	Prevalence of visiting doctor, male, heavy smokers intending to quit: 0.138% Pre-Quit rate: 9.02% After-Quit rate (male) 9.02%×1.84=16.60% Quit rate increased =16.60%-9.02%=7.58% After-intervention smoking prevalence=0.138%-	6.92	0.752%	0.810%-0.752%=0.058%	94

		7.58%×0.138%=0.128%				
	Female (CPD≤10)	Prevalence of visiting female smokers intending to quit: 0.102% Pre-Quit rate: 19.70% After-Quit rate 19.70%×1.84=36.25% Quit rate increased =36.25%-19.70%=16.55% After-intervention smoking prevalence=0.102%-16.55%×0.102%=0.085%	2.08	0.092%	0.110%-0.092%=0.018%	14
	Female (11<CPD<19)	Prevalence of visiting doctor, male, medium smokers intending to quit: 0.056% Pre-Quit rate: 9.73% After-Quit rate (male) 9.73%×1.84=17.90% Quit rate increased =17.90%-9.73%=8.17% After-intervention smoking prevalence=0.056%-8.17%×0.056%=0.051%	3.59	0.132%	0.145%-0.132%=0.013%	10
	Female (CPD>20)	Prevalence of visiting doctor, male, heavy smokers intending to quit: 0.007% Pre-Quit rate: 9.02% After-Quit rate (male) 9.02%×1.84=16.60% Quit rate increased =16.60%-9.02%=7.58% After-intervention smoking prevalence=0.007%-7.58%×0.007%=0.006%	6.92	0.036%	0.041%-0.036%=0.005%	5
Sub-total	**Light Smokers**					550
	Medium Smokers					350
	Heavy Smokers					99
Total						999

Scenario 4: Counselling among the Smokers plus NRT patch CPD>10

		Values of Smoking Prevalence used in PAF calculation	Values of Relative Risk of Lung Cancer Used in PAF Calculation	Population Attributable Fraction(PAF) to Lung Cancer	Pre-After Discrepancy	
					%	**Life saved**
Pre-Intervention	**Male (11<CPD<19)**	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Male smokers intending to quit 17.95% Male smokers intending to quit AND 10<CPD<19 (medium smoker) 33.80% Prevalence of visiting male smokers intending to quit: 49.2%×35.4%×17.95%×33.80%=1.057%	3.59	2.665%	/	/
	Male (CPD>20)	Male: 49.2% [1] Male smokers visiting doctor: 35.40% Male smokers intending to quit 17.95% Male smokers intending to quit AND CPD>=20 (heavy smoker) 4.40% Prevalence of visiting doctor male heavy smokers intending to quit: 49.2%×35.4%×17.95%×4.40%=0.138%	6.92	0.810%	/	/
	Female (11<CPD<19)	Female: 2.6% [1] Female smokers visiting doctor: 35.40% Female smokers intending to quit 17.95% Prevalence of visiting female smokers intending to quit: 2.6%×35.4%×17.95%×33.80%=0.056%	3.59	0.145%	/	/
	Female (CPD>20)	Female: 2.6% [1] Female smokers visiting doctor: 35.40% Female smokers intending to quit 17.95% Female smokers intending to quit AND CPD>=20 (heavy smoker) 4.40% Prevalence of visiting female heavy smokers intending to quit: 2.6%×35.4%×17.95%×4.40%=0.007%	6.92	0.041%	/	/

After-intervention	**Male (11<CPD<19)**	Pre-Prevalence: 1.057% Pre-Quit rate (male): 9.73% [4] After-Quit rate (male) 9.73%×1.84×1.7=30.44% Quit rate increased =30.44%-9.73%=20.71% After-intervention smoking prevalence=1.057%-20.71%×1.057%=0.838%	3.59	2.124%	2.665%-2.124%=0.541%	160,991×0.541%=871
	Male (CPD>20)	Pre-Prevalence: 0.138% Pre-Quit rate (male): 9.02% After-Quit rate (male) 9.02%×1.84×1.7=28.21% Quit rate increased =28.21%-9.02%=19.19% After-intervention smoking prevalence=0.138%-19.19%×0.138%=0.112%	6.92	0.659%	0.810%-0.659%=0.151%	160,991×0.151%=243
	Female (11<CPD<19)	Pre-Prevalence:0.056% Pre-Quit rate: 9.73% [4] After-Quit rate (female) 9.73%×1.84×1.7=30.44% Quit rate increased =30.44%-9.73%=20.71% After-intervention smoking prevalence=0.056%-20.71%×0.056%=0.044%	3.59	0.114%	0.145%-0.114%=0.031%	77,773×0.031%=24
	Female (CPD>20)	Pre-Prevalence:0.007% Pre-Quit rate: 9.02% After-Quit rate (female) 9.02%×1.84×1.7=28.21% Quit rate increased =28.21%-9.02%=19.19% After-intervention smoking prevalence=0.007%-19.19%×0.007%=0.0057%	6.92	0.034%	0.041%-0.034%=0.007%	77,773×0.007%=5

Total Life Saved						1,143

Table 4.11: Results of Effectiveness of Impact of Physician Counselling and NRT Patch Implemented in Healthcare System on the Lung Cancer Disease Burden in China

#	Scenario	Subjects	Covered smoking population (in million)	Additional Quitter Generate		Avoided Lung Cancer Death	
				Total	**Per million smokers receiving service**	**Total**	**Per million smokers receiving service**
1	**Brief Counselling**	All smokers visiting doctor	128.3×35.40%=45.42	**2.35 million**	0.05 million	1,654	36
2	**Motivational Interview**	All smokers visiting doctors and NOT intending to quit	128.3×35.40%×82.05%=37.27	**0.70 million**	0.02 million	534	14
3	**Intensive Counselling**	Smokers visiting doctors AND intending to quit	**Light smoker** : 128.3×35.40%×17.95%×61.80%=5.04	**0.85 million**	0.17 million	Light (CPD≤10):550	109
			Medium/heavy smoker: 128.3×35.40%×17.95%×38.20%=3.11	**0.26 million**	0.08 million	Medium/heavy (CPD>10): 449	144
	Sub-total		128.3×35.40%×17.95%=8.15	**1.11 million**	0.14 million	999	123

4	**Intensive counselling plus NRT patch**	Smokers (CPD>10) visiting doctors AND intending to quit	128.3×35.40%×17.95%×38.20%=3.11	**0.65 million**	0.21 million	1,143	367

Table 4.12: Alternative Effectiveness OR on Sensitivity Analysis

#	Scenario	Effectiveness	
		By length	**By provider**
1	**Brief counselling to ALL smokers**	/	/
2	**Motivational interview to ALL smokers NOT intending to quit;**	/	3.49 (1.53 -7.94) (primary care physicians)
3	**Intensive counselling to ALL smokers intending to quit**	2.22 (1.84, 2.68) (multiple follow up sessions)	/
4	**Intensive counselling to only the smokers intending to quit AND being medium/heavy smokers (CPD>10).**	Additional support of NRT patch in clinical setting: 1.84 (1.65, 2.06)	/

Table 4.13: Sensitivity Results of Effectiveness of Impact of Physician Counselling and NRT Patch Implemented in Healthcare System on Lung Cancer Disease Burden in China

#	Scenario	Odds Ratio	Covered smoking population (in million)	Additional Quitter Generated		Avoided Lung Cancer Death	
				Total	**Per million smokers receiving service**	**Total**	**Per million smokers receiving service**

2	**Motivational Interview** All smokers visiting doctors and NOT intending to quit	3.49 (1.53 - 7.94) (primary care physicians)	128.3×35.40%×82.05%=37.27	**6.42million**	0.17 million	5,076	136
3	**Intensive Counselling** Smokers visiting doctors AND intending to quit	2.22 (1.84, 2.68) (multiple follow up sessions)	**Light smoker** : 128.3×35.40%×17.95%×61.80%=5.04	**1.23million**	0.24 million	Light (CPD≤10): 799	159
			Medium/heavy smoker: 128.3×35.40%×17.95%×38.20%=3.11	**0.37million**	0.12 million	Medium/heavy (CPD>10): 655	211
	Sub-total		128.3×35.40%×17.95%=8.15	**1.60million**	0.20 million	1,454	179
4	**Intensive counselling plus NRT patch** Smokers (CPD>10) visiting doctors AND intending to quit	Additional support of NRT patch in clinical setting: 1.84 (1.65, 2.06)	128.3×35.40%×17.95%×38.20%=3.11	**0.73million**	0.23 million	1,291	415

4.2.2 Sensitivity Analyses on Effectiveness of Physician Counselling and NRT

Sensitivity analyses were conducted by varying the effectiveness based on the ranges of the definitions of well-established physician counselling and NRT. The intervention costs were recalculated accordingly.

The effectiveness of motivational interview, brief physician counselling, intensive physician counselling were drawn from the most recent Cochrane Reviews, which are systematic reviews of primary research in health care and health policy, and are recognised worldwide as the highest standard in evidence-based health care. In order to accurately estimate the potential impact of lung cancer burden, a sensitivity analysis was conducted by selecting alternative effectiveness values of physician counselling by length (one session vs. multiple sessions) and providers (general provider vs. physician-specific). In addition, since the NRT patch is available both by over the counter and prescription in US, therefore, sensitivity analyses were also conducted by specific effectiveness reported in clinical settings. The sensitivity analysis on effectiveness of four scenarios is listed in Table 6.13.

4.2.3 Summary of Effectiveness of Physician Counselling and NRT Patch in China

Brief counselling (Scenario 1) is the most straightforward smoking intervention with well-established effectiveness among the four designed scenarios. Given that brief counselling usually lasts 3 to 10 minutes and is usually provided in the healthcare system, therefore, there is little major variation in the effectiveness of brief counselling. No additional sensitivity analysis on the effectiveness of brief counselling was thus conducted.

The results indicated if all 45.42 million current smokers in urban China----including all light, medium, and heavy smokers as well as smokers both intending to quit and not intending to quit, are provided brief counselling during their doctor visit, smoking prevalence among male and female would reduce 0.88% and 0.05%, respectively, which represented a total of 2.35 million additional quitters, or 0.05 million quitters per million smokers receiving brief counselling service (Table 4.10). In addition, the results from the Comparative Risk Assessment (CRA) Model indicated a total of 1,654 lung cancer death (36 deaths per million smokers receiving service) would be avoided.

Results of Motivational Interview (Scenario 2) showed a wide range of additional quitters generated and total lung cancer deaths avoided when different effectiveness values were applied. Meta-analysis evidence has shown the overall odds ratio of motivational interview is 1.27, in contrast, the odds ratio of motivational interview provided by primary physician in healthcare system is 3.49, which is significantly higher than the general odds ratio of motivational interview. So, the odds ratios of 1.27 and 3.49 were both applied into the calculation.

The results indicate that if a total of 37.27 million current smokers in urban China who did NOT intend to quit were provided a motivational interview during their doctor visit, a total of 0.70 million to 6.42 million NOT intending to quit smokers would quit smoking, and approximately 534 to 5,076 lung cancer deaths could be possibly avoided (Table 4.11 & Table 4.13).

If intensive counselling (Scenario 3) was provided to a total of 8.15 million smokers intending to quit during their doctor visit, the results show that a total 1.11 million to 1.60 million smokers intending to quit would quit smoking, and that 999 to 1,454 lung cancer deaths could be saved in this smoking group when applied general effectiveness (OR: 1.84) and effectiveness conducted for intensive counselling with multiple sessions only (OR: 2.22).

When the impact of intensive counselling by light smokers (CPD<10) and medium/heavy smokers (CPD≥10) were investigated separately, the results show that intensive counselling had a greater impact on light smokers on the total additional quitters generated than the avoided lung cancer deaths. A total of 0.85 to 1.23 million light smokers would quit and 550 to 799 lung cancer deaths would be avoided, relative to 0.26 to 0.37 million quitters generated and 449 to 655 lung cancer deaths avoided among medium/heavy smokers (Table 4.11 & Table 4.13).

If an NRT patch was provided adjunct to intensive counselling to the medium/heavy smokers who intend to quit (Scenario 4), approximately 0.65 to 0.73 million medium/heavy smokers would quit and 1,143 to 1,291 lung cancer death would be avoided, which suggests that an additional 0.36 to 0.39 million quitters may be generated and another 636 to 694 lung cancer deaths avoided relative to intensive counselling only among medium/heavy smokers who intend to quit (Table 4.11 & Table 4.13).

Among the four scenarios, providing brief counselling to all smokers (Scenario 1) during their doctor visit would help the greatest number of smokers receiving the service to quit (2.35 million). Results show that brief counselling to all smokers visiting doctor is the most consistent and had the greatest impact on smoking cessation in the healthcare system in urban China. In contrast, providing intensive counselling to medium/heavy smokers produces the least number of quitters (0.26 –0.37 million) in the healthcare system in China, but when provided adjunct with NRT patch, the total number of quitter produced significantly increased (0.65—0.73 million). Providing intensive counselling among light smokers (producing 0.85—1.23million quitters) had greater impact than medium/heavy smokers (producing 0.26—0.73 million quitters), and even shown larger effect than medium/heavy smokers when they are provided NRT patch with intensive counselling (0.65—0.73 million)

Because the much higher relative risks of lung cancer among medium/heavy smokers (OR=3.59 for medium smokers; 6.92 for heavy smokers) relative to light smokers (OR=2.08), the results of CRA model suggested different pattern of avoiding lung cancer death based on effect by per unit smoking population. Intensive counselling helped to avoid more lung cancer deaths among medium/heavy smokers (144-211 per million smokers) than light smokers (109-159 per million smokers). When medium/ heavy smokers were provided NRT patch with intensive counselling, the effect of avoiding lung cancer death increased approximately two times (367-415 per million smokers) than providing intensive counselling only.

Overall, when we look at the additional quitters generated and avoided lung cancer death per unit population, such as per million smokers receiving the services, the effectiveness of four scenarios in China suggested similar pattern of that in Western countries. Intensive physician counselling plus NRT patch (Scenario 4) is the most effective smoking cessation intervention in healthcare setting, followed by intensive physician counselling only; brief counselling intervention, and motivational interview.

4.2.4 Economic Evaluations of Implementation of Physician Counselling and NRT in China

Currently, the average cost of smoking-attributable lung cancer is not available in China. According to most recent research evidence in China (Yang, 2011c), there were a total 154,745 of urban smoking population who died from cancer, and lung cancer was the number one smoking-attributable cancer among both male and female smokers, accounting for approximately 75% of total smoking-attributable cancer. Therefore, the average cancer cost for each smoking patient was used as the estimate of average lung cancer cost in the following calculation (Table 4.14 & Table 4.15).

Table 4.14 Economic Costs of Smoking in Urban China in 2008 (in US$1000)

	Direct Medical Cost	Indirect Cost (Transportation, Absence	Total

		from Work, Indirect Mortality Cost)	
Total	2 ,835, 055	10, 679, 942	13, 514, 997
Per Death	18.32	69.02	87.34

Exchange rate of the Chinese Yuan against US$¼U6.9451 in 2008 based on China Statistical Yearbook, 2009.

Table 4.15 Economic Saving on Physician Counselling and NRT in 2008 in Healthcare System in Urban China

#	Scenario	Covered Subjects	Covered smoking population (million)	Annual Avoided Lung Cancer Death	Medical cost saved (in US million)	Indirect Mortality cost saved (in US million)	Total cost saved (in US million)
1	**Brief Counselling**	All smokers visiting doctor	45.42	1,654	30.30	114.16	144.46
2	**Motivational Interview**	All smokers visiting doctors and NOT intending to quit	37.27	534	9.78	36.86	46.64
3	**Intensive Counselling**	Smokers visiting doctors and intending to quit	5.04 (light smoker)	550	10.08	37.96	48.04
			3.11 (medium/heavy smoker)	449	8.23	30.99	39.22
	Sub-total		8.15	999	18.31	68.95	87.26
4	**Intensive counselling plus NRT patch**	Medium/heavy smokers (CPD>10) visiting doctors and intending to quit	3.11	1,143	20.94	78.89	99.83

The economic analysis was conducted by calculating the cost per additional quitter, total cost spending on implementing each scenario, and total cost saving from avoided lung cancer deaths from each scenario.

According China salary yearbook 2009, healthcare system employees' annual salary is $5,135 (or RMB 35,662) (http://www.yearbookinfo.net/zgtjnj/html/E0416c.htm). The total working days for a government-owned enterprise, including hospitals, is 251 days/year; thereby, the salary per minute was approximately $0.04 per minute in 2008. This estimate does not include any additional overhead or management costs.

The total costs of each scenario were calculated by multiplying the unit cost spent on each covered smoker to the total covered smoking population. The unit cost for patient for physician counselling was estimated by multiplying physician's per minute salary to the total time spent on each patient. For scenario 4, the NRT patch cost for each patient was calculated by multiplying the average retail price of NRT patch to the total NRT patch recommended by US clinical guidelines of treating tobacco dependence (Fiore, 2008).

When taking into consideration economic costs, the cost-effectiveness patterns presented were different from that which only examined effectiveness. Counselling length and retail price for NRT patch are two major variables affecting intervention costs. Counselling lengths, most commonly used in Western literature, and the current retail price of the NRT patch in China were both used in the economic calculations.

The effectiveness of physician counselling and NRT, affected by quit rates for corresponding smoking population and relative risks of lung cancer, differed from cost-effectiveness, which was also highly associated with the "cost" of implementing each scenario. More specifically, in this study the cost included the salary of physician and local retail price of the NRT patch.

The overall economic analysis results suggest cost savings for all scenarios that included physician counselling (Scenario 1 to 3), with brief counselling (Scenario 1) as the most cost saving scenario. Given the high retail price of NRT in China, the economic analysis results show that Scenario 4 of intensive counselling plus NRT required an additional $200 million in financial investments.

The economic analysis also estimated the cost per quitter across scenarios by dividing the total cost by the total quitters generated by that scenario. Briefly speaking, the pattern of cost for each quitter was consistent with the cost-effective pattern among the four scenarios (Table 4.16 A and Table 4.16 B), which suggests that brief counselling (Scenario 1) required the least financial investment for each quitter ($2.23 to $7.73), followed by intensive counselling (Scenario 3) ($5.80 to $23.49) and motivational interview (Scenario 2) ($31.94 to $95.94). When the NRT cost was involved (Scenario 4), the cost per quitter significantly increased to $466.78 to $478.27.

Among the four scenarios, motivational interview was the one with the greatest variation in effectiveness and cost-effectiveness. The other three scenarios showed a consistent pattern on either effectiveness or cost-effectiveness.

Table 4.16 (A): Cost Spending and Saving on Implementation Physician Counselling and NRT in Urban China:

#	Scenario	Covered smokers (in million)	Cost Spending				Cost Saving		Total Net Saving (in US million)
			Cost components	Cost per patient	Total cost spending (in US million)	Cost per quitter	Avoided lung cancer death annual	Cost Saving (in US million)	
1	**Brief Counselling**	45.42	Counselling time (3-10 min for each selected smoker)	$0.04/min ×3min =$0.12	$5.45	$2.32	1,654	$144.46	$139.01
				$0.04/min ×10min=$0.4	$18.17	$7.73			$126.29
2	**Motivational Interview**	37.27	Counselling time (15-45 min for each selected smoker)	$0.04/min ×15min=$0.60	$22.36	$31.94	534	$46.64	$24.28
				$0.04/min ×45min=$1.80	$67.09	$95.84			$-20.45
3	**Intensive Counselling**	5.04 (light smoker)	Counselling time (20-80 min for each selected smoker)	$0.04/min ×20min=$0.80	$4.03	$4.74	550	$48.04	$44.01
				$0.04/min ×80min=$3.20	$16.13	$18.97			$31.91
		3.11 (medium/heavy smoker)			$2.49	$9.58	449	$39.22	$36.73
					$9.95	$38.27			$29.27
	Sub-total	8.15		20min	$6.52	$5.87	999	$87.26	$80.74
				80min	$26.08	$23.49			$61.18

4	**Intensive counselling plus NRT patch**	3.11	Counselling time (20-80 min for each selected smoker); NRT retail price	Cost for NRT patch: $1.72 per patch ×56 (8weeks use)=$96.76 $0.04×20=$0.80 Total cost: $96.76+$0.80=$97.56	$303.41	$466.78	1,143	$99.83	$-203.58
				Cost for NRT patch: $1.72 per patch ×56 (8weeks use)=$96.76 $0.04×80=$3.20 Total cost: $96.76+$3.20=$99.96	$310.86	$478.27			$-211.03

Table 4.16 (B): Sensitivity Results of Cost of Physician Counselling and NRT Patch Implemented in Healthcare System on Lung Cancer Disease Burden in China:

<table>
<tr><th rowspan="2">#</th><th rowspan="2">Scenario</th><th rowspan="2">Covered smokers (in million)</th><th colspan="4">Cost Spending</th><th colspan="2">Cost Saving</th><th rowspan="2">Total Net Saving (in US million)</th></tr>
<tr><th>Cost components</th><th>Cost per patient</th><th>Total cost spending (in US million)</th><th>Cost per quitter</th><th>Avoided lung cancer death annual</th><th>Cost Saving (in US million)</th></tr>
<tr><td rowspan="2">2</td><td rowspan="2">Motivational Interview</td><td rowspan="2">37.27</td><td rowspan="2">Counselling time (15-45 min for each selected smoker)</td><td>$0.04/min ×15min=$0.60</td><td>$22.36</td><td>$3.48</td><td rowspan="2">5,076</td><td rowspan="2">$443.34</td><td>$420.98</td></tr>
<tr><td>$0.04/min ×45min=$1.80</td><td>$67.09</td><td>$10.45</td><td>$376.25</td></tr>
<tr><td rowspan="6">3</td><td rowspan="4">Intensive Counselling</td><td rowspan="2">5.04 (light smoker)</td><td rowspan="4">Counselling time (20-80 min for each selected smoker)</td><td rowspan="4">$0.04/min ×20min=$0.80

$0.04/min ×80min=$3.20</td><td>$4.03</td><td>$3.28</td><td rowspan="2">Light (CPD≤10):799</td><td rowspan="2">$69.78</td><td>$65.75</td></tr>
<tr><td>$16.13</td><td>$13.11</td><td>$53.65</td></tr>
<tr><td rowspan="2">3.11 (medium/heavy smoker)</td><td>$2.49</td><td>$6.73</td><td rowspan="2">Medium/heavy (CPD>10):655</td><td rowspan="2">$57.21</td><td>$54.72</td></tr>
<tr><td>$9.95</td><td>$26.89</td><td>$47.26</td></tr>
<tr><td rowspan="2">Sub-total</td><td rowspan="2">8.15</td><td rowspan="2"></td><td>20min</td><td>$6.52</td><td>$4.08</td><td rowspan="2">1,454</td><td rowspan="2">$126.99</td><td>$120.47</td></tr>
<tr><td>80min</td><td>$26.08</td><td>$16.30</td><td>$100.91</td></tr>
</table>

4	**Intensive counselling plus NRT patch**	3.11	Counselling time (20-80 min for each selected smoker); NRT retail price	Cost for NRT patch: $1.72 per patch ×56 (8weeks use)=$96.76 $0.04×20=$0.80 Total cost: $96.76+$0.80=$97.56	$303.41	$415.63	1,291	$112.76	$-190.65
				Cost for NRT patch: $1.72 per patch ×56 (8weeks use)=$96.76 $0.04×80=$3.20 Total cost: $96.76+$3.20=$99.96	310.86	$425.84			$-198.1

Chapter 5 Discussion

The economic evaluation of smoking cessation interventions is aimed at identifying interventions that use the fewest resources and that are most effective in reducing both the number of smokers and smoking-related diseases, including lung cancer, coronary heart disease, COPD, myocardial infarction, and stroke (Flack, Taylor, & Trueman, 2007). Currently, a number of tobacco treatments used in Western healthcare systems, ranging from clinician advice to medication, have proven to be clinically effective and cost-effective in relation to other medical interventions, such as treatment of hypertension and hyperlipidemia and other preventive interventions including periodic mammography (Maciosek, Coffield, & Edwards, 2006; Quist-Paulsen, Lydersen, & Bakke, 2006; Shearer, & Shanahan, 2006; Solberg, Maciosek, & Edwards, 2006). Because of their favourable return on investment, smoking cessation interventions in Western countries have been widely regarded as the "gold standard" of cost-effectiveness from a societal perspective (Fiore et al., 2008; Foulds, 2002; Javitz, Swan, & Zbikowski, 2004; Warner, Mendez, & Smith, 2004).

However, the cost-effectiveness of smoking cessation interventions is highly context specific. Although the efficacy of a variety of smoking cessation interventions are well-established (Baska, Straka, Baskova, & Mad'ar, 2004; Cummings, Fix, Celestino, Carlin-Menter, O'Connor, & Hyland, 2006; Johansson, Tillgren, Guldbrandsson, & Lindholm, 2005; Kaper, Wagena, Severens, & Van-Schayck, 2005; Miller, & Wood, 2003; Song, Raftery,& Aveyard, 2002), the cost of smoking cessation interventions vary considerably depending on the context, including the retail price for NRT products and the salary levels of healthcare professionals. Therefore, the cost-effectiveness of cessation interventions may be very different across countries (Hall, Lightwood, Humfleet, Bostrom, Reus, & Munoz, 2005;Halpin, McMenami, Rideout, & Boyce-Smith, 2006). Currently, existing economic evaluations of smoking cessation interventions have mostly been conducted in Western countries. Few economic evaluations have been conducted in low- and middle-income countries where financial resources are more limited. In order to optimally allocate resources, evidence on local cost-effectiveness studies in low- and middle-countries is urgently needed. With the rapidly increasing economic burden of smoking-attributable disease, China is facing the financial challenge of how to best allocate resources to widely promote smoking cessation interventions for a reduction in the economic burden caused by smoking-attributable disease. However, the cost-effectiveness of smoking cessation interventions in China remains unknown.

To our knowledge, the present study provides the first data on the potential effectiveness and cost-effectiveness of physician counselling and NRT patch use among Chinese smokers. Study 1 examined patterns of smoking and quitting among Chinese smokers, as well as visits to physicians. Study 2 used the findings from Study 1 to investigate the effectiveness and cost-effectiveness of implementing physician counselling and NRT patches on the disease burden of lung cancer in healthcare system in urban China.

5.1 Smoking and Quitting in Urban China

Study 1 revealed that, despite the high smoking prevalence in China, the proportion of current smokers visiting doctors annually is low. Approximately one-third of smokers (35.4%) visited a doctor in the past year, an estimate that is much lower compared to Western countries where approximately 70-80% of adult smokers visit their physician each year (Curry et al., 2007; Curry et al., 2008; Fiore et al., 2008,). Research from previous waves of the ITC China Survey found that 33.6% smokers reported visiting a doctor in the past year, reflecting a consistent low proportion of smokers visiting doctor in China (Yang et al., 2010). The low proportion of smokers in urban China visiting their doctor might be due to two reasons. First, China is still in the early stages of the smoking epidemic and has not yet experienced the peak of smoking-attributable disease burden. Many smokers have yet to experience smoking-attributable health effects, which would consequently increase visits to the doctor. As a result, one might expect the proportion of doctor visits among smokers to increase in the future as the looming health burden becomes a reality. Second, the low rate of doctor visits among smokers most likely reflects the current healthcare system and limited access to healthcare services. A report from the WHO (2000) indicated that among its 191 member countries, China's healthcare system ranked 188th in terms of access to healthcare, equality and financial investment. By 2003, only approximately 20% of urban population and 10% of rural population were covered by medical insurance (Ministry of Health, 2004). According to the China National Health Surveys, between 1998 and 2003, the proportion of people getting sick in the last two weeks but not visiting their doctor due to financial reasons increased rapidly in both urban and rural areas (Ministry of Health, 2004). Therefore, the low proportion of smokers visiting doctor also might be due to both the low proportion of smokers visiting healthcare system and overall less access to the healthcare system at population-level in China.

Results from Study 1 also indicated that the smokers who visited their doctor were significantly more likely to quit smoking than their counterparts who did not report visiting a doctor (OR=1.53; 95%CI=1.10-2.13). This finding is consistent with the previous national study showing that among former smokers, being sick was the number one reason for them to quit (Yang et al., 2001). Since there are no smoking cessation interventions routinely available in the healthcare system in China, the higher quit rate among sick smokers simply reflects the fact that Chinese smokers were more self-motivated to quit smoking due to illness, rather than the doctor's visit per se having an effect.

Third, Study 1 found that, among the smokers who visited a doctor, males and female smokers reported similar intentions to quit smoking. Results from a previous national study showed similar overall patterns in intention to quit among male and female smokers in China (Yang et al., 2001). In addition, when the quit rates were further examined among light, medium/heavy smokers separately by intention to quit, the results still showed no significant differences among all the comparisons ($p>0.05$ for all the cases). Therefore, although smoking prevalence is much higher among males than females in China (49.2% vs. 2.4%), they demonstrate very similar quitting patterns, including intention to quit, visits to the doctor, and quit rates.

In summary, the results of Study 1 suggests there are three patterns among smokers in urban China: (1) Chinese smokers had a low proportion of visiting doctors annually relative to smokers in Western countries; (2) smokers visiting doctors were more likely to quit; and, (3) there were no statistically significant gender differences in quitting rates among smokers visiting doctors in intention to quit and cigarette consumption.

5.2 Potential Effectiveness and Cost-Effectiveness of Smoking Cessation Interventions in Urban China

Based on the results of Study 1, four well-established smoking cessation interventions (Scenario 1 to 4) in Western countries were examined to explore their potential effectiveness and cost-effectiveness. The health outcomes used to measure effectiveness and cost-effectiveness of the four smoking cessation interventions were the number of additional quitters generated and avoided lung cancer deaths.

5.2.1 Brief Counselling

Implementing brief counselling to all smokers (Scenario 1) in the healthcare system in urban China was the most effective and cost-effective among the four smoking cessation interventions. Results indicated that implementing 3-10 min brief counselling to total of 45.42 million smokers visiting the healthcare system in urban China could potentially increase the quit rate by 5.07%, producing a total 2.35 million additional quitters at average cost at $2.32-7.73 per quitter, depending on the minimum (3 minute) and maximum (10 minute) resource spending on counselling, resulting in a total of $114.16 to $144.46 million of total savings (discrepancy between total cost of implementation brief counselling relative to the total saving from avoided lung cancer deaths).

5.2.2 Motivational Interview

Among all the counselling scenarios (Scenario 1 to 3), the results of motivational interviewing among the smokers not intending to quit (Scenario 2) demonstrated the greatest range of effectiveness. When applied to the general effectiveness of motivational interview (OR=1.27), the total number of quitters produced was 0.70 million; however, the effectiveness of motivational interviewing provided by primary physician (OR=3.49) was almost three times higher compared with the general effectiveness, resulting in a total of 6.42 million quitters. The cost per quitter was estimated as $31.94 to $95.84 if only 0.70 million quitters were produced, but sharply decreased to $3.48 to $10.45 per quitter based on 6.42 million total quitters.

Research consistently shows the majority of Chinese smokers have no intention of quitting smoking, varying from 72% to 75% (Yang et al., 2011; Yang et al., 2001; Yang et al., 2005). Study 1 estimated that approximately 85% of current smokers did not intend to quit, demonstrating that the situation of smoking cessation in China has not improved and that it might have even grown worse. The low proportion of smokers in China who intend to quit makes motivational interviewing an appropriate strategy for China in theory. However, the broad variation of both effectiveness and cost-effectiveness patterns provided little reliability for real-world practice.

5.2.3 Intensive Counselling

Compared with brief counselling, intensive counselling to smokers intending to quit (Scenario 3) generated a total of 1.11 to 1.60 million additional quitters at the cost per quitter of $4.08 to $23.49 depending on the length of intensive counselling. However, intensive counselling had a different impact on light smokers (CPD≤10) and medium/heavy smokers (CPD>10). In absolute terms, intensive counselling produced more quitters among light smokers (0.85 to 1.23 million) at an average cost of $3.28 to $18.97 per quitter, relative to that among medium/heavy smokers (0.26 to 0.37 million) at a cost $6.73 to $38.28 per quitter. The economic analysis suggested a total cost saving of $29.27 to $36.73 million on the avoided lung cancer deaths in medium/heavy smokers. In contrast, among light smokers, the short length of intensive counselling results in total cost saving of $31.91 to 44.01 million on lung cancer deaths.

Intensive counselling produced more quitters among light smokers, but avoided fewer lung cancer deaths compared with medium/heavy smokers. The different results are mainly due to the different pre-intervention quit rates and relative risks of lung cancer among light smokers and medium/heavy smokers. The pre-intervention quit rate was significantly higher in light smokers (19.70%) than medium/heavy smokers (9.73%/9.02%); hence, after multiplying effectiveness of intensive counselling (OR), the discrepancy between pre- and after- intervention was much larger among light smokers, resulting in a greater impact on smoking cessation. However, from a cost-effectiveness perspective, the relative risk of smoking-attributable lung cancer is the major contributor. In China, evidence shows that the relative risk of smoking-attributable lung cancer among light, medium and heavy smokers was 2.08, 3.59, 6.92, respectively (Liu et al., 1998). The significantly higher lung cancer risk in medium/heavy smokers means that intensive counselling would avoid a relatively greater number of smoking-attributable lung cancer deaths among medium/heavy smokers.

5.2.4 Intensive Counselling plus NRT Patch

The fourth scenario explored the effectiveness and cost-effectiveness of NRT patch use in addition to intensive counselling only (Scenario 3). Providing NRT patches to medium/heavy smokers who intend to quit doubled the number quitters, for a total of 0.65—0.73 million quitters, relative to their counterparts who only received intensive counselling in Scenario 3, which shows 0.26 to 0.37 million quitters. However, when costs are taken into account, the pattern changed. The cost of each quitter increased significantly from $9.58 to $38.28 for intensive counselling only, to $466.7 to $478.27 when the NRT patch was involved. The results are comparable to the findings from a recent US meta-analysis, which estimated the average costs per quitter for NRT and counselling as $260 to $2330 (Kaper, et al., 2005). NRT patch plus intensive counselling was the only scenario that did not result in a net monetary benefit relative to cost of avoided lung cancer deaths among the four designed scenarios. The main reason for the negative monetary benefit is due to the high NRT patch retail price in the Chinese market.

The relatively high cost for smoking cessation is not only true in China, but also in other countries. Evidence from Western countries suggests that, compared with the cost of pharmacies being involved in smoking cessation interventions, physicians' salaries do not account for a significant proportion between the various pharmacological therapies, including both over the counter and prescription NRT provision (Cornuz et al., 2003). Another study conducted in the Seychelles identified medication prices as a substantial factor in cost analysis, particularly in developing countries where prices may be dependent on local production, licensing, infrastructure capacity, technology requirements, and capital investment (Gilbert, 2004).

Besides the high retail price, NRT is not widely accepted in China, nor considered as an effective and viable smoking cessation aid among Chinese smokers due to limited awareness and marketing of these products (Lam et al., 2005; Zhong, 2009). In a local study (Lam et al., 2005), found that when NRT products were provided at no charge, approximately two thirds (66%) of respondents either refused to use or did not finish the free sample. Recent research evidence from China indicated that, given the high NRT retail price and low levels of NRT marketing in China, few Chinese smokers regarded NRT as an effective and viable smoking cessation aid (Zhong, 2009).

The current perception and patterns of NRT use among Chinese smokers is similar to the experience of Western countries. In Western countries, NRT was introduced into healthcare systems by prescription in early 1990's. The introduction of NRT patches was accompanied by strong marketing campaigns, targeted at both smokers and health professionals, encouraging use of the NRT patch as a "proven and effective" smoking cessation strategy. Marketing materials included information on which group of smokers should be offered NRT, in what dose, and whether NRT is effective when used alone or together with some form of additional support strategy (Saul, 1993). Despite significant increases in use, research suggests that some smokers still hold false beliefs about the efficacy and safety of NRT. For example, approximately two-thirds of US smokers report a false belief about NRT (Cumming, 2004). The experience of NRT promotion in Western countries provides a useful reference for the developing countries.

In summary, the results of Study 2 show that brief counselling is the most effective and cost-effective smoking cessation intervention. Intensive counselling for light smokers intending to quit also demonstrated strong evidence of effectiveness and cost-effectiveness. Due to the large intervals of effectiveness and cost-effectiveness, motivational interviewing should be considered a lower priority. The high cost and low acceptance of NRT in China suggest that there are considerable barriers to promoting NRT at present.

By converting health outcome measures into monetary value, economic evaluations of smoking cessation interventions not only allow for comparisons between smoking cessation interventions, but also to other health interventions. For example, the results of the present study provided cost-effectiveness evidence by calculating cost per quitter for each hypothetical scenario, which allows straightforward comparisons among the four smoking cessation interventions. On the other hand, this study also explored the cost analysis on physician counselling and NRT implementation as well as the avoided cost on decreased lung cancer deaths by the four smoking cessation interventions; this could be used to compare cost of implementing that intervention to determine which one is less expensive.

The lack of standardization in methodology of available economic evaluation is the biggest challenge for comparing the cost-effectiveness results across the available data. Existing economic evaluations of smoking cessation interventions vary considerably in their approach and evaluation methods (e.g., differences in study designs, outcome measures, and cost components). Differences in measure definition and estimation, discount rates, model assumptions, and research perspectives not only affect the research findings, but also limit comparisons across different interventions. This diversity also makes it difficult to determine which of the different program characteristics (e.g., target populations and intervention types) caused one intervention to appear more cost-effective than others. More broadly, when different countries are involved, the costs of material, human resources, and medication retail price critical for cost calculations cause additional difficulties in interpreting cost-effectiveness findings to different countries.

5.3 Cost-Effectiveness Comparisons across Countries

The findings of this study in China are consistent with research in Western countries. Evidence from Western countries indicates that intervention effectiveness, natural quit rate, and the salary of the intervention providers have the strongest influences on cost-effectiveness (Cornuz, 2006). However, when medication is involved, pharmacotherapy price has a stronger influence on the cost-effectiveness ratio than physicians' time since it comprises a larger proportion of the total cost of the intervention. The pharmacy price is particularly important in the cost calculation for developing countries because the retail price of pharmacotherapy may be dependent on local production, licensing, infrastructure capacity, technology requirement and capital investment (Gilbert, Pinget, Bovet, Cornuz, & Shamlaye, 2004). Compared with Western countries, the salary levels paid in China's healthcare system are generally low. Compared with physicians' hourly rate of $67 in Canada, $83 in France, $108 in US, and $134 in UK in 2003, the hourly rate in China was only $2.40 in 2009. The low hourly rate is a primary factor in the high cost-effectiveness of smoking cessation counselling in healthcare system in urban China. The average retail price of an 8-week supply of NRT patches is $96.76. In the US, the retail price for the same supply of NRT patches is reportedly $88, similar to the retail price in China (Cumming, Hyland, Carlin-Menter, Mahoney, Willett, & Juster, 2011). In contrast, the retail price of an 8-week of NRT supply in Australia is approximately $430 (Shearer et al., 2006), which is significantly higher than in both China and the US. It should be noted, however, that the costs of NRT in most Western countries has recently dropped considerably due to the availability of generics. In Korea, the retail price of an 8-week NRT supply was approximately $70 in 2009 (Oh, Lim, Yun, Shin, & Park, 2012). Therefore, the retail price of NRT in China is comparable to other countries. Taken together with the low salary level in China healthcare system and comparable NRT retail price, the cost of physician counselling would not be a major barrier to widely promote smoking cessation interventions.

The broader literature from Western countries also suggests that smoking cessation interventions, ranging from clinician advice to NRT, have been compared favourably with other common healthcare interventions, such as medical treatment of hypertension and hyperlipidemia and to other preventive interventions such as heart disease prevention programs (Cromwell, Bartosch, Fiore, Hasselblad, & Baker 1997; Quist-Paulsen et al., 2006; Shearer et al., 2006). In a study conducted in Switzerland, Cornuz and colleagues (2003) found NRT was not only more cost-effective relative than pharmacological hypertension treatments in Switzerland, but also compared favourably with hypertension treatments in UK, Canada, and the US. Because of their favourable return on investment, smoking cessation programs are regarded as the gold standard of cost-effectiveness in health care (Fiore et al., 2008).

5.4 Cost-Effectiveness of Smoking Interventions in China

In China, economic evaluations of smoking cessation interventions and other healthcare programs are very limited. In addition to comparing smoking cessation interventions to other medical procedures, comparisons can also be made with other tobacco control policies, such as tobacco taxation. In recent years, after China ratified the FCTC in 2005, the Chinese government increased tobacco tax as the first step of toward using population-level tobacco control interventions. From a public health perspective, the “costs” of increasing cigarette tax are essentially zero; instead, tax increases could increase revenue and the healthcare cost savings could offset the potential costs borne by smokers. On the other hand, a large body of research evidence has established that increasing the price (via tax) of cigarettes encourages quitting, prevents smoking initiation, and reduces cigarette consumption (USDHHS, 2000). The levels of cigarette taxes vary across countries. Taxes tend to be absolutely higher and also account for a greater share of price (two-thirds or more) in high-income countries. In middle/low income countries, taxes are generally much lower, and they account for less than half of the price of cigarettes. China currently levies a 38% tax at the retail-level, a relatively low rate compared to cigarette tax rates around the world, the median of which is about 60% (Mackay, & Eriksen, 2002)

The price elasticity of cigarette is an economic term measuring the effect of change in cigarette's price on changes in its consumption. For example, if cigarette price elasticity is -0.10, this means when cigarette price increases 10%, the consumption would decrease 1%. Therefore, the larger price elasticity suggests the bigger effect of increasing price. The existing research evidence suggests different estimations of cigarette price elasticity of demand between high-income countries and middle/low income countries. Overall, the cigarette price elasticity in high-income countries is -0.25 to -0.50 while in low/middle income countries is -0.50 to -1.00 (Chaloupka, Hu, Warner, Jacobs, & Yurekli, 2000), indicating smokers in low/middle countries had more sensitive response to cigarette price than smokers in high-income countries. In China, the 2002 National Smoking Prevalence Survey showed an overall price elasticity of -0.16, meaning a 10% increase in the price of cigarettes would lead to a 1.6% reduction in cigarette consumption (Hu, 2008). The low price elasticity in China shows that Chinese smokers are less sensitive not only relative to other low/middle income countries, but also compared to high-income countries. The wide range of cigarette prices in China (from $0.15 to $24.4 per pack) provides great flexibility for Chinese smokers to switch to lower priced brands without either reducing cigarette consumption or quitting. The most recent Chinese tax increase on cigarettes in May 2009 was absorbed by manufacturers and did not affect cigarette retail price. Therefore, despite the fact that tobacco taxation is the most cost-effective tobacco control measure, it has had relatively little effect on smoking cessation in China.

5.5 Strengths and Limitations

5.5.1 Strengths

To authors' best knowledge, the present study is the first study to explore the effectiveness and cost-effectiveness of physician counselling and NRT in China at the population level. Study 1 provides recent data on visiting doctors, intention to quit, and cigarette consumption among Chinese smokers. Data on the relative risks of smoking-attributable lung cancer and effectiveness of physician counselling and NRT patch were drawn from the best available evidence in China where available, as well as from Western countries.

5.5.2 Limitations

Study 1: The six participating cities in ITC China survey were selected based on geographical representativeness and levels of economic development; however, they are not theoretically representative of urban China in terms of sampling theory (Wu et al, 2010). Therefore, the results should be interpreted with caution. In addition, due to the low smoking prevalence among females in China, the ITC sample included only 200 female smokers, compared with 3600 male smokers. The analysis based on the female sample should also be interpreted with caution.

Study 2: The major limitation of the Study 2 was data availability. There are several well-developed mathematical simulation models that are often applied in cost-effectiveness of smoking cessation studies, including Benefits of Smoking Cessation on Outcomes (BENESCO) model, Health Economic Consequences of Smoking (HECOS) model; the PREVENT model, and the Chronic Disease Model (CDM). However, these models require detailed data on smoking/quitting behaviour as well as relative risks of mortality and morbidity of smoking-attributable disease (Bolin, 2012). In China, although smoking prevalence data is well-established, the relative risks for the major smoking-attributable diseases by various categories, such as geographic areas, gender and age, are not well-established. Particularly, for some smoking-attributable diseases such as respiratory disease, the long latency period results in a significant difference between relative risks of mortality and morbidity. The lack of data on subgroups in China for many of these health effects makes cost-effectiveness research on smoking cessation difficult. The lack of data in China means that certain standardized measures in Western countries could not be estimated, such as years of life saved, i.e., the quality-adjusted life year (QALY) and the disability-adjusted life year (DALY).

The second limitation of Study 2 is the underestimation of cost-effectiveness. A wide range of diseases is known to be attributable to smoking. Due to data limitations, this study only used lung cancer cost in estimates of the effectiveness and cost-effectiveness of the most popular smoking cessation interventions. Therefore, the estimates in the current study drastically underestimate the actual cost-effectiveness on smoking-attributable diseases. For example, major smoking-attributable diseases among Chinese smokers, such as COPD and cardiovascular disease responsible for approximately one-third of smoking-attributable death in China (Gu et al., 2009) were not taken into account in the present study. In addition, the study did not take the significant disease burden from second-hand smoke into account. Recent estimates from Global Adult Tobacco Survey (Yang et al., 2010) indicated that there is a total of 556 million of non-smokers aged 15 years older who were exposed to second-hand smoking in China, accounting for 72.4% of the general population of 15 years older. The total number of non-smokers affected by second-hand smoke has been greater than the number of current smokers. Therefore, the effects of second-hand smoke are substantial, and the effectiveness and cost-effectiveness of physician counselling and NRT patch have been underestimated in China.

The lack of standardization in methodology across economic evaluations represents a challenge for comparing cost-effectiveness results across studies. Existing economic evaluations of smoking cessation interventions vary considerably in their approach and evaluation methods (e.g., differences in study designs, outcome measures, and cost components). Differences in definition of measures and estimation, discount rates, model assumptions, and research perspectives not only affect the research findings, but also limit comparing across different interventions. This diversity also makes it difficult to determine which of the different program characteristics caused one intervention to appear more cost-effective than others. When different countries are involved, the costs of material, human resources, and medication retail price are critical for cost calculations, causing additional difficult in interpreting cost-effectiveness findings to different countries.

Because the infrastructure costs of smoking cessation programs, such as the cost of training physicians, were not included, the cost of smoking cessation interventions appear to be understated in the calculations.

Chapter 6 Implications

The results of this study provide strong support for introducing smoking cessation counselling, particularly brief counselling, into the healthcare system in China.

If these results are to be translated into a public health benefit, even a single application of any brief or intensive physician counselling (Scenario 1 to 3) that produce only a small effect on quit rates could potentially have an enormous public health impact in China. However, questions remain about the extent to which physician counselling could be effectively implemented in China. In Western countries, after several decades smoking cessation campaign, it is reported that approximately 40% to 70% physicians provide smoking cessation advice to their smoking patients (Longo et al., 2006; CTUMS, 2006). In China, evidence has shown that less than 20% of Chinese physicians provided specific smoking cessation assistance to their smoking patients, including counselling, self-help materials, quit-smoking medications, or follow-up support (Hu, 2003; Young et al., 2001). Physicians who received training on smoking cessation (Lancaster et al., 2000; Stead et al., 2009; Twardella et al., 2005),and have positive attitudes toward smoking cessation (Vogt et al., 2005) have higher engagement levels to effectively deliver smoking cessation intervention. Therefore, training on smoking cessation for physicians is a necessary strategy to implement smoking cessation in the healthcare system in urban China. An important early goal might be reducing the smoking prevalence among male physicians since the lack of knowledge by physicians negatively impacts quit rates of patients.

It is important to note that although the use of more intensive interventions (i.e., longer sessions, more sessions) may produce enhanced abstinence rates, these interventions may have limited reach, affecting fewer smokers, and may not be feasible in some primary care settings. For instance, not all smokers are interested in participating in an intensive intervention, and not all smokers may have access to or can afford services that can provide intensive interventions.

With one-third of the world's smokers, tobacco control in China is crucial to global efforts to reduce the smoking-attributable disease burden. If the smoking-attributable disease burden in second smokers is also taken into account, tobacco control is even more urgent and important. Research on tobacco control in China will be of great importance to other developing countries because China shares many of the social and economic challenges facing other developing countries.

Tobacco control in China is facing an economic and public health crossroads. China is the world's largest tobacco consumer and producer with a state-owned tobacco monopoly. With rapidly increasing smoking-attributable burden worldwide, particularly in developing countries, the looming public health burden provides a powerful incentive for policy makers to launch initiatives to lower smoking rates.

Preventing smoking initiation and helping a current smoker to quit are two major tobacco control strategies. Successful tobacco control programs that focus on discouraging a non-smoker to smoke will affect the smoking-attributable disease burden in forty years, whereas smoking-attributable mortality in the near future or throughout the first half of 21st century will be determined by rates of smoking cessation among current smokers (Peto, Lopez, Boreham, Thun, Heath, & Doll, 1996). The research evidence from several high-income countries, including Sweden, UK, and Germany all found that the annual number of smoking-attributable deaths still increased in recent years despite a reduction in the prevalence of smoking over the last 30 years (Bolin, Borgman, Gip, & Wilson, 2011). Smoking cessation interventions are urgently needed in China in order to avoid the upcoming peak of smoking-attributable disease burden.

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Appendix A: Summary of Evidence on Smoking Prevalence in China

Study	Sample	Definition of Smoking	Findings on Smoking Prevalence
Smoking cessation in China: findings from the 1996 national prevalence survey (Yang et al, 1999) Project: the 1996 National Prevalence Survey Yang G (1999). Smoking in China: findings of the 1996 national prevalence survey. JAMA 1999; 282:1247–1253.	National representative sample of 122 220 people aged 15–69 years.	Ever-smokers: persons who had ever smoked for at least 6 months; Current smokers: smoking tobacco products at the time of the survey Heavy smokers: smoked at least 20 cigarettes daily	Ever smoking rate: 66.9% for men and 4.2% for women, with an overall prevalence of 37.6%; Current smoking rate: 63% for men,3.8% for the women, for an overall prevalence of 35.3%; Heavy smoking: 7.5% for men and 0.2% for women were heavy smokers. The average cigarettes smoked per day by male smokers were about 2 per day at ages 15 to 19 years; 12 per day at 20 to 25 years; 15 cigarettes per day by age 30 years and above. Female smokers smoked slightly more than 10 cigarettes per day.
Smoking and passive smoking in Chinese, 2002 (Yang et al., 2005) Project: Surveillance on risk behaviors conducted in 2002 Yang GH (2005) Smoking and passive smoking in Chinese, 2002 Zhonghua Liu Xing Bing Xue Za Zhi. 2005 Feb;26(2):77-83	National representative sample of 16 056 respondents aged 15-69 years.	Ever-smokers: persons who had ever smoked for at least 100 cigarettes in the lifetime; Current smokers: smoking tobacco products in the past 30 days;	Ever-smoking rate: 66.0% for men and 3.08% for women, with an overall prevalence of 35.8%; Current smoking rate: 57.4% for men, 2.6% for the women, for an overall prevalence of 31.4%; The average cigarettes smoked per day by male smokers were 15 cigarettes per day. Female smokers smoked slightly more than 10 cigarettes per day. Smokers at age group of 40-59 had highest cigarette consumption at approximate 16 cigarettes per day.
Trends in smoking and quitting in China from 1993 to 2003: National Health Service Survey data. (Qian et al., 2010) Project: National Health Service Surveys conducted in 1993, 1998 and	National representative sample. The surveys conducted in all 31 provinces in mainland China. The 1993 survey interviewed 55 000 households, 215 163 respondents. The 1998 survey interviewed 57 000	Ever smokers: the respondents who either smoked at the time of the survey or who had previously smoked but had quit at the survey time; Current smokers: the respondents reporting smoked at the time of the	Ever-smoking rate: (1) 1998 survey year: 57.4% for men and 4.5% for women, with an overall prevalence of 31.1%; (2) 2003 survey year: 52.1% for men and 3.5% for women, with an overall prevalence of 27.7%; *1993 ever smoking rate was not reported in the study; Current smoking rate: (1) 1993 survey year: 59.6% for

2003 Qian J. et al. (2010) Trends in smoking and quitting in China from 1993 to 2003: National Health Service Survey data. Bull World Health Organ. 2010 Oct 1;88(10):769-76. Epub 2010 Apr 16.	households, 216 101 respondents. The 2003 survey interviewed 57 000 households, 193 698 respondents. All respondents were 15 years older.	survey and who had smoked at least 100 cigarettes during their lifetime; Heavy smokers: smoked at least 20 cigarettes daily	men, 5.1% for the women, for an overall prevalence of 32.2%; (2) 1998 survey year: 53.4% for men, 4.0% for the women, for an overall prevalence of 28.9%; (3) 2003 survey year: 48.9% for men, 3.2% for the women, for an overall prevalence of 26.0%; Heavy smoking: (1) 1998 survey year: 26% for men, 16% for the women, for an overall prevalence of 25.6%; (2) 2003 survey year: 53% for men, 29% for the women, for an overall prevalence of 51.3%; Average cigarette consumption per day among smokers was not reported.
Prevalence of smoking in China in 2010 (Li et al., 2011) Project: Global Adult Tobacco Survey (GATS) conducted in 2010 Prevalence of smoking in China in 2010 (Li et al., 2011) N Engl J Med. 2011 Jun 23;364(25):246924-70.	National representative sample of 13,354 adults aged 15 years older.	Current smoker: respondents who self-identified as “currently smoking”, including daily use or less than daily use.	Current smoking rate: 52.9% for men, 2.4% for women, for an overall prevalence of 28.1%. Average cigarette consumption per day among smokers was 14.3 among male smokers and 10.6 among female smokers, with overall 14.2 cigarette per day among male and female smokers.

Appendix B: Summary of Evidence on Relative Risks of Lung Cancer Caused by Smoking

Study	Type	Research Smoking Group	Reference group	Results of Relative Risk	Chi-square trend
Combined analysis of case control studies of smoking and lung cancer in China (Yu et al., 1996)	Meta-analysis *(urban only)*	Male	Non-smoker	3.01 (2.36-3.46)	P<0.001
		Female	Non-smoker	2.32 (2.02-2.66)	
		Squamous	Non-smoker	4.79(4.02-5.70)	P<0.001
		Adenocarcinoma	Non-smoker	1.02 (0.87-1.20)	
		Daily cigarette consumption <10	Non-smoker	1.24 (0.87-1.76)	P<0.01
		Daily cigarette consumption 10-19	Non-smoker	2.19 (1.43-2.79)	
		Daily cigarette consumption >=20	Non-smoker	4.47 (2.79-7.17)	
		Smoking duration less than 30 years	Non-smoker	1.10 (0.62-1.16)	P<0.01
		Smoking duration more than 30 years	Non-smoker	2.49 (1.73-3.57)	
		Mortality/Death	Non-smoker	2.33 (2.02-2.68)	P>0.05
		Incidence/New case	Non-smoker	2.13 (1.94-2.34)	
The hazards and benefits associated with smoking and smoking cessation in Asia: a meta-analysis of prospective studies (Nakamura et al., 2009)	Meta-analysis *(general report including both urban and rural)*	Current smoker	Never smoker	2.78 (1.63-4.75)	N/A
		Former smoker	Never smoker	1.96 (1.38-2.79)	
Smoking and Lung Cancer in China: Combined Analysis of Eight Case-Control Studies (Liu, 1992)	Combined analysis of eight case-control studies *(urban only)*	Male	Non-smoker	3.09 (2.61-3.66)	N/A
		Female	Non-smoker	2.30 (1.96-2.69)	
		Daily cigarette consumption <10	Non-smoker	1.03 (0.79-1.34)	P = 0.000001
		Daily cigarette consumption 10-19	Non-smoker	2.04 (1.66-2.54)	
		Daily cigarette consumption >20	Non-smoker	3.33 (2.69-4.21)	
		Smoking duration less than 30 years	Non-Smoker	1.02 (0.78-1.33)	P = 0.000001
		Smoking duration more than 30 years	Non-smoker	2.66 (2.20-3.22)	
Mortality Attributable to Smoking in China (Gu et al., 2009)	Prospective cohort study in a national representative sample of 169,871 Chinese adults aged 40 or older *(general report including both*	Male (cigarette consumption <16 pack year)	Non-smoker	1.10 (1.03-1.17)	P<0.001
		Male (cigarette consumption 16-30 pack year)	Non-smoker	1.18 (1.12–1.23)	
		Male (cigarette consumption >30 pack year)	Non-smoker	1.26 (1.20–1.33)	
		Female (cigarette consumption <16 pack year)	Non-smoker	1.22 (1.13–1.33)	P<0.001
		Female (cigarette consumption 16-30 pack year)	Non-smoker	1.29 (1.17–1.42)	
		Female (cigarette consumption >30 pack year)	Non-smoker	1.38 (1.25–1.53)	

	urban and rural)				
Age-related Effects of Smoking on Lung Cancer Mortality: A Nationwide Case-Control Comparison in 103 Population Centers in China (Jiang et al., 2008)	A nationwide retrospective case control study among 69 million adults aged 35 years older *(general report including both urban and rural)*	Male (cigarette consumption <10 pack year)	Non-smoker	1.77 (1.70 to 1.85)	P<0.001
		Male (cigarette consumption 10-19 pack year)	Non-smoker	1.92 (1.83 to 2.01)	
		Male (cigarette consumption 20-29 pack year)	Non-smoker	2.55 (2.45 to 2.67)	
		Male (cigarette consumption 30-39 pack year)	Non-smoker	3.62 (3.46 to 3.79)	
		Male (cigarette consumption 40-49 pack year)	Non-smoker	4.68 (4.47 to 4.80)	
		Male (cigarette consumption >50 pack year)	Non-smoker	6.29 (5.99 to 6.60)	
		Female (cigarette consumption <10 pack year)	Non-smoker	2.59 (2.45 to 2.74)	P<0.001
		Female (cigarette consumption 10-19 pack year)	Non-smoker	3.01 (2.81 to 3.22)	
		Female (cigarette consumption 20-29 pack year)	Non-smoker	3.41 (3.18 to 3.66)	
		Female (cigarette consumption 30-39 pack year)	Non-smoker	5.78 (5.29 to 6.32)	
		Female (cigarette consumption 40-49 pack year)	Non-smoker	6.22 (5.67 to 6.82)	
		Female (cigarette consumption >50 pack year)	Non-smoker	7.51 (6.80 to 8.29)	
Emerging tobacco hazards in China: 1. Retrospective proportional mortality study of one million deaths (Liu et al., 1998)	Retrospective cohort study of one million death *(urban and rural reported separately)*	Male	Non-smoker	2.98(SE:0.05)	N/A
		Female	Non-smoker	3.24(SE: 0.06)	
		Daily cigarette consumption <10	Non-smoker	2.08 (SE:0.05)	
		Daily cigarette consumption 10-19	Non-smoker	3.59 (SE:0.06)	
		Daily cigarette consumption >=20	Non-smoker	6.92 (SE:0.14)	

Appendix C: Summary of Effectiveness of NRT Products

Source	Study Type	Timeline of Reported Findings	Nicotine Gum OR (95%CI)	Nicotine Patch OR (95%CI)	Nicotine Nasal spray (OR (95%CI)	Inhaler OR (95%CI)	Sublingual tablet or lozenge OR (95%CI)	Overall OR (95%CI) (if applicable)
Silagy C et al. (2006)	Meta-Analysis	6-12 months	1.66 (1.51-1.81)	1.84 (1.65-2.06)	2.35 (1.63-3.38)	2.14 (1.44-3.18)	2.05 (1.62-2.59)	1.77 (1.66-1.88)
Fiore MC. et al. (2008)	Meta-Analysis	6 months	1.50 (1.2-1.7) (6-14 weeks) 2.20 (1.5-3.2) (longer than 14 weeks)	1.9 (1.7- 2.3) For both 6-14 weeks use or longer than 14 weeks 2.3 (1.7-3.0) For high dose for both standard and long term use	2.3 (1.7-3.0)	2.1 (1.5-2.9)	Not reported	Not reported
Eisenberg MJ, et al. (2008)	Meta-Analysis	6-12 months	1.65 (1.37-2.01)	1.88 (1.60–2.22)	2.37 (1.57–3.60)	2.18 (1.38–3.45)	2.06 (1.47–2.87)	Not reported
Wu P. et al. (2006)	Meta-Analysis	12 months	1.60 (1.37-1.86)	1.63 (1.41-1.89)	Not reported	Not reported	Not reported	1.71 (1.55-1.88)

Appendix D: Summary of Available NRT Research Evidence in China

Study	Study Design	Subject	Treatment course	Abstinence rate	Abstinence measure
Sun, et al. 2009 (Bei Jing)	Randomized Controlled Trial	A total of 211 adult smokers who smoked ≥ 10 cigarettes per day for at least 1 year	12 weeks Nicotine Tablet 2mg/tablet * Behaviour counselling was provided to both groups as supplement	52% vs. 19% (Nicotine tablet group vs. placebo group)	Sustained abstinence at 3 month follow-up
Yu et al., 2006 (Bei Jing)	Randomized Controlled Trial	A total of 60 adult smokers who smoked ≥ 15 cigarettes per day for at least 1 year	7 weeks Nicotine Patch Dose not available	35% vs. 52% (Nicotine patch vs. Nicotine patch + behaviour counselling)	Sustained abstinence at 12 weeks follow-up
Yang et al., 2010 (Six cities of China)	Population study	A total of 995 adult smokers Average cigarette daily consumption not reported	Not available	Not available	Point abstinence (non-smoking at 18 month follow-up)
Lam, et al. 2005 (Hong Kong)	Population study	1186 adult smokers Average cigarette per day=18 (72% of respondents smoked≥10 cigarettes per day)	8 week Nicotine patch (78%), nicotine gum (12%), nicotine inhaler (4%), combination of any two (6%) Dose not available * Behaviour counselling was provided to all respondents as supplement	40% vs. 25% (NRT group vs. non-NRT group)	Point abstinence (7 days non-smoking at 12 month follow-up)
Abdullah, et al. 2008 (Hong Kong)	Population study	365 elderly smokers 30% of participants≥10 cigarettes per day)	Minimum 4 weeks Type and dose of nicotine product used in the study not available * Behaviour counselling was provided to all respondents as supplement	Not available	Point abstinence (7 days non-smoking at 6 month follow-up)

Abdullah, et al. 2006 (Hong Kong)	Population study	129 young smokers under 24 Average cigarette per day=12 (46% of respondents smoked≥10 cigarettes per day)	Minimum 4 weeks Type and dose of nicotine product used in the study not available * Behaviour counselling was provided to all respondents as supplement	60% vs. 16% (NRT group vs. non NRT group)	Point abstinence (7 days non-smoking at 12 month follow-up)